

**THE APPLICATION OF MARKOV AND SEMI-
MARKOV MODELS TO THE CONTROL OF
CATARRH AND LEPROSY DISEASES**

BY

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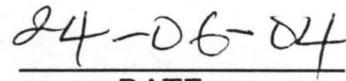
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DECLARATION

I hereby declare that the research work embodied in this thesis is an original work carried out by me. It has never been presented elsewhere for the award of any degree. All works related to the field of study, prior to the present studies have been duly acknowledged and referred.



ABUBAKAR USMAN YUSUF



DATE

DEDICATION

To my son, Abubakar, my late father Abubakar, my wife Hajara and to my late mother Hajara and of course the entire family.

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Glory be to God who has given us the opportunity to accomplish this research work.

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ABSTRACT

A study on the application of Markov and Semi-Markov modeling for the control of Catarrh and leprosy diseases have been reported in this thesis. The models incorporate the concept of preventive/curative treatment and also the effect of seasonal variation on the catarrh disease. Exponential and Weibull probability distribution functions were used to describe the time a leprosy patient stays in each state of the models. The models were considered also for the both the discrete and continuous times. The minimum cost of control of the diseases was obtained through the Markov reward model. It was found that catarrh disease is not seasonal. The continuous time models for Semi-Markov performed better than the discrete time. A contrast of the two probability functions showed that the exponential function is better and it is easily handled. The cost model showed that it is cheaper in the long run to visit a medical doctor and to use high priced drugs than self-care and low priced drugs.

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CHAPTER ONE

1.0 INTRODUCTION

1.1 BACKGROUND TO THE STUDY

It is a popular saying that health is wealth; in other words, good health is wealth. This statement perhaps may not have much meaning to a man that is in a good condition of health until he falls sick and becomes ill, it is then and only then he can realise the usefulness of good health. Lack of good health is a state of ill health. Poor health is caused by a disease. A disease is an illness, a disorder of the body and/or of the mind, Macqueen (1985).

The main causes of disease are small organisms. They are so small that we cannot see them with the naked eye. These organisms include viruses, bacteria and parasitic worms. Many diseases exist in the human world. Some diseases are common to people that live in the tropical part of the world and they are called tropical diseases.

Catarrh and Leprosy are some of the diseases that are common in the tropics. Catarrh is one of the diseases that many people do not take seriously. This is because they believe that Catarrh is not an independent disease on its own. Thus, they think that Catarrh is a sign or a symptom of some other diseases. Consequently, Catarrh does degenerate to one or two other diseases in many patients, because, it has not been given the desired recognition and attention.

Leprosy disease means different things to many people including some of the elites. To some people, Leprosy is a hereditary disease. That is, parents

simply pass it on to their off-spring at birth. But, to some other people, the disease is not only hereditary; it also cannot be treated or cured.

It is very important not only to be aware of these diseases but also to be able to exercise the God-given power and authority to cure them. There are two ways by which a man can control these diseases. It is often said that prevention is better than cure. A man can be given a preventive treatment so that he does not become infected with a disease. It is also an important practice that a man is given curative treatment so that he can recover from a disease with which he has become infected.

1.2 MARKOV AND SEMI – MARKOV PROCESSES

Andrei Andreivich Markov (1856 – 1922) a Russian Mathematician, is recognized as the 'inventor of Markov chains. The basic concept of Markov processes is that of "state " of a system and state "transition". It is a process that runs in time. A Markov process in discrete state and time is called a Markov Chain. When the particular set of states have been specified it is necessary to record the probability of change from one state to another during a unit of time. This information can be shown in a 'directed graph' called transition diagram and recorded in the transition matrix which is a stochastic matrix.

The Markov chain requires the process to change state or remain in the same state at the appropriate time units. Therefore, we consider a situation where transition occurs at several units of time.

This leads to the general form of Markov process called the semi-Markov process. Simply put, a semi-Markov process is that process that

depends on the transition probability matrix P_{ij} and holding time matrix $h(t)$ (where, $i, j = 1, 2, 3, \dots$ denote states). These two parameters form the input data for the interval transition probabilities $Q_{ij}(n)$ where $n = 0, 1, 2, \dots$ representing time.

1.3 JUSTIFICATION

Mathematical models can be categorized broadly as being probabilistic or deterministic. Among situations where probabilistic models are more suitable, very often a better representation is given by considering a collection or a family of random variables instead of a single one. A collection of random variables that are indexed by a parameter such as time and space is known as stochastic process (or 'random' or 'chance' process). Markov processes form a sub-class of stochastic processes with highly simplified assumptions and a wide range of applications including recovery, relapse and death due to diseases.

Catarrh and leprosy diseases have been used to provide illustrations to these models. We also wish to create a greater awareness on the readers about these diseases by modeling.

These models can be used as a predictive device for studying the health status of catarrh and leprosy patients. The predictions will be useful to the doctors, hospital administrators, policy makers and the general public.

1.4 THE OBJECTIVE OF THE STUDY

- (i) The primary objective of the study is to develop a mathematical model using the principles of Markov chain and semi – Markov.

processes for the control of catarrh and leprosy diseases. The other objectives are:

- (ii) To model the seasonal effect on the catarrh disease using the two major seasons in Nigeria.
- (iii) To determine specifically the degree of effectiveness of the treatment using the models on the sensitivity analysis (optimal degree of effectiveness).
- (iv) To make a comparison of the discrete and the continuous time cases as well as the two distribution functions; the exponential and the Weibull.
- (v) To educate the general public on diseases used in the models and to further impress and inspire the possible application of Markov process to other fields of study.
- (vi) To determine the optimal costs of control analytically using the principle of Markov decision processes.

1.5 PROBLEM OF THE STUDY

The existing models do not help us to determine the control of leprosy in the future on the basis of the present level of control. We therefore intend to develop a model to predict the control of disease in the future on the basis of present level of control.

As for the catarrh disease there is no quantitative result as for whether or not catarrh disease is seasonal. These are the fundamental problems these models are designed to solve.

1.6 SIGNIFICANCE OF THE STUDY

The models are predictive tools for studying the progression of catarrh and leprosy diseases. These results are important information to the patients, Government and non – governmental organizations that are concerned about the control of these diseases.

1.7 SCOPE OF THE STUDY

Although, the models have potential for general application to diseases and the related processes, we have limited our study to catarrh and leprosy diseases

1.8 LAYOUT OF THESIS

The work presented in this thesis covers the research carried out by the author and it is presented as follows:

A discussion of the background to the study, including the justification and the objectives is followed by a review of related literature consisting of the application of simple mathematical techniques to the study of diseases with the epidemic of the Hippocrates (459-377BC). Later development in this area of research resulted in the more complex deterministic equations, the chain-binomial and the stochastic techniques or the simulations. Catarrh, Leprosy and the major seasons in Nigeria are then presented.

One of the important simplified assumptions of Markov and Semi-Markov techniques is that, the time the process stays in a state should be described by a function of probability distribution. The exponential and Weibull probability distributions are the probability functions for this process. They

have been discussed, including the introductory materials in the theory of Markov and Semi-Markov processes.

Markov and Semi-Markov techniques constitute the tools for the formulation and development of the models. These models are simple theoretical frameworks to study Catarrh and Leprosy cases. They are subjected to verification or illustrations using data, be it live data or hypothetical data, for a better understanding and clarity.

The conclusions and summary of the work as well as the areas that require further investigation are finally presented.

CHAPTER TWO

2.0 REVIEW OF LITERATURE

2.1 MODELLING FOR THE CONTROL OF DISEASE

In this chapter, we present a brief historical account of modelling for the control of diseases, the growth and development of mathematical theories of the spread of diseases is given. We also present the deterministic and stochastic analytic models. The most recent scientific approach of simulation modelling is presented. We also discuss the modelling approach used in this project. The leprosy and catarrh diseases were also discussed including the seasonal variations in Nigeria.

2.2 THE BEGINNING OF THE MATHEMATICAL MODELLING OF DISEASES.

The modelling of diseases started as far back as the ancient Greeks, with the epidemics of Hippocrates (459 - 377 BC), Bailey (1975). John (1620 - 1674) and William Petty (1623 - 1687) could be considered as pioneers of medical statistics and the understanding of large-scale phenomena connected with disease and mortality, but the time was not ripe for anything approaching a connected theory of epidemics. This was because the requisite mathematical techniques were themselves only then in the process of development. Another reason was the insufficient knowledge about the spread of disease. A good start was made in the field of mechanics and astronomy more than 200 years before any real progress was achieved in the Biological Sciences (Bailey,

1975). Daniel Bernoulli in 1760 used mathematical methods to assess the effectiveness of inoculation against small pox, with a view to influencing public health policy.

The major feature of the beginning of modern scientific achievement in this field was the rise of the science of bacteriology in the 19th century. The work of Pasteur) and Koch involved mainly the statistical appraisal of records showing the incidence and locality of known cases of diseases, Bailey (1975).

The work of Farr was mathematically sophisticated. He fitted a normal curve to quarterly data on deaths from smallpox. Brownlee used a similar method to predict the course of outbreak of rinderpest amongst cattle. The curve was fitted to four rising successive monthly totals and extrapolated values used for prediction. Although observed and predicted curves were both bell-shaped, agreement in detail was not very good.

The work of Farr and Brownlee involved more of curve fitting and prediction. Deterministic and stochastic models were developed in the early part of the 20th century Bailey(1975) Generally, there are three modelling approaches for disease control: Deterministic, Analytical stochastic, and Simulation, usually stochastic.

2.3 DETERMINISTIC MODELLING

Ross(1911) presented a mathematical model for malaria, which attempted to take into account a set of measures describing various aspects of transmission. The study of respiratory disease using a deterministic approach to the heterogeneity of spread of infection was provided by Becker and Hopper

in 1983. An epidemiological application of sophisticated control theoretic model was provided by Hethcote (1983).

The age-dependent immunisation model was designed to predict appropriate strategies for disease control. Hethcote utilised data on measles and rubella to determine vaccination strategies appropriate for their control at various levels of immunisation coverage.

2.4 STOCHASTIC MODELLING

Deterministic models soon lost their popularity because of their inability to accurately describe recurrent cycles of disease (Bailey 1982). When data became more extensive and much smaller groups were considered, elements of "chance and variation" became more prominent. Mckendrick (1926) was the first to construct stochastic models of epidemic processes. Greenwood gave an alternative probability treatment five years later (Bailey, 1975)

"Continuous infection" and "chain binomial" stochastic models were introduced next. These probability models were more appropriate for dealing with smaller groups in which random variation would play a larger role. Although these models achieved popularity they are usually mathematically and computationally more complex than the simple deterministic models.

Stochastic models now appear more frequently in the study of diseases (Bailey, 1975). Kimber and Crowder (1984) proposed a model to analyse resistance times to infection under treatment. A general stochastic model was proposed by Hillis (1979).

Several stochastic models have been presented to describe distributions of infectious disease over time and space. Goldacre (1977) attempted an

analysis of meningitis using space-time clustering techniques introduced by Knox (1964) to detect the existence of factors associated with infection.

Trend surface analysis, a polynomial regression technique developed for use in geology, was applied to small pox data from Brazil Angulo (1977) to determine if general trends in what appeared to be random spatial patterns could be detected. A centrifugal pattern emerging from the center of a city and spreading outwards was detected. Box-Jenkins models, variants of the ARIMA (Autoregressive Integrated Moving Average) models utilized in economics, were applied to infection of Chickenpox. Time-series data also provided the data base for models of epidemic velocity proposed by Cliff and Haggett (1982).

The etiology of disease is of primary concern to many epidemiologists and can be seen either in a deterministic or stochastic framework. A deterministic perspective is one in which factor x causes y if (all other factors being held constant) a change in the value of x results in a change in the values of y , in a completely prescribed way tracing out a mathematical function of some form. In practice, probability theory and statistical techniques are used to assess evidence regarding causality. In any causal analysis of data, the goal is to account for variation in the dependent variable.

Several models of this sort have been utilized to analyze data in studies of infectious diseases, including most commonly linear regression, log-linear analysis, logistic regression, discriminant analysis, and proportional hazards modelling. An example is the work of Stevens and Lee (1978) who used a generation effect model to assess the impact of anti-tubercular chemotherapy on mortality. The generation effect model assumes that the mortality pattern for

each cohort is set early in life; rates vary only according to birth cohort. This model was used to project current mortality experience using past cohort data. The large differences noted by Stevens and Lee (1978) between the expected and the observed rates were ascribed to the effect of intervention with chemotherapy.

Discriminant analysis was used to study chronic obstructive pulmonary disease (Lebowitz and Burrows, 1977). Linear regression models were utilized for analysis of risk associated with influenza mortality (Clifford et al, 1977). A model of risk factors in a non-infectious disease, skin cancer, has been constructed using logistic regression (Vitaliano, 1978). The following year, log-linear models were used to analyze data from cohort study of acute respiratory illness (Melia et al, 1979).

Markov chain models have been applied to study the progression of disease. Fix and Neyman (1951) constructed a simple stochastic model of recovery, relapse, death and loss of patients. They are concerned with the difference in effect either of the same treatment applied to different categories of patients or of different treatments applied to a specified category of patients. In all cases the criterion for comparison was the frequency of surviving specified periods of time. That model was used to study the effects of treatment of cancer of the breast. Marshall and Goldhammer (1955) applied Markov processes to study the epidemiology of mental disease. Markov chain models have also been constructed to study the effect of weather on asthma (Jains, 1986 and Jain R.K. 1988). Similar studies have been reported in Roberts et al (1990), Sacks et al (1977), Sargent (1991), Schenzled et al (1979), Anderson et al (1991), Shahani et al (1987) and Shahani (1981).

Many disease models have yielded valuable information and more information is still being sought to meet the demand of dynamics of diseases and complexities. However, Mathematical modelling is more suitable for very simple systems that allow high simplifying assumptions and not for systems that involve uncertainty, complexity and scarce resources. In such cases simulation models are often appropriate and preferable.

2.5 SIMULATION MODELLING

Simulation is a process for studying or finding a solution for a problem, or calculating the effect of a course of action, by representing it in mathematical terms, especially using the computer, (Readers' Digest Universal Dictionary, 1989). A simulation model is an abstract model which represents some system in the real world. Simulation methods have developed since the 1960s and may well be the most commonly used of all the analytical tools of management science (Pidd, 1992).

Complete fade-out of infection may occur in sufficiently small communities if fresh cases are not introduced, whereas, in communities above a certain critical size it will merely happen that infection reaches a low level before building up again for a fresh outbreak (Anderson and May, 1982). These conclusions are in agreement with observed data and with the results of empirical investigations using Monte Carlo methods in conjunction with the electronic computer. A computer simulation study was conducted in the area of recurrent epidemics and endemicity with special reference to the interpretation

of real public health measles data, Bartlett (1961). This perhaps marks the beginning of the use of computer simulation.

Computerized simulations have been extremely valuable in elucidating the properties of multi-state models of disease and in shedding light on proposed intervention strategies. Extensive studies of this type have been made in tuberculosis control by Waaler, Geser and Anderson (1962).

Another area of some public health consequence is the interference and interaction phenomena that may occur between different disease organisms. Lila Elveback and her co-workers have developed a series of six fundamental models of increasing complexity that can be used for the study (by computerised simulations) of public health control of poliomyelitis by means of live polio vaccine, including the situation where effect of the vaccine is inhibited by enterovirous infections. The chief reference is (Elveback, Fox, and Varma, 1964).

Simulation modelling is a very attractive powerful method for dealing with the complications of a variety of diseases including asthma. A Simulation model for managing asthma has been reported in Shahani et al. (1994).

The evolution of modern (more powerful, less expensive and easier to use) computers and high level languages has popularized (Zeigler, 1979) the application of simulation for solving real-life problems in several descriptions, and the expected advances in computer technology indicate that this trend will continue.

2.6 A REVIEW OF LEPROSY MODELS

There has been a widespread use of statistical techniques in clinical trials and in attempting to determine variables which are relevant to the epidemiology of leprosy, but the application of Operational Research techniques to the study of leprosy has been minimal.

Bechelli adopted the kinship coefficient in his study of the correlation between leprosy rates in villages different distances apart, Bechelli (1973). According to him, given n villages V_i ($i = 1, 2, \dots, n$) the i^{th} village having population W_i and a gene frequency P_i for one genetic marker, the kinship coefficient between all villages at distance x from each other is estimated by

$$\psi_{(x)}P = \frac{\sum \frac{W_i W_j}{W_i W_j} (P_i - P)(P_j - P)}{P(1 - P) \frac{W_i W_j}{W_i W_j}}$$

where P is the average gene frequency for all villages separated by distance x , and the summation is extended over all village pairs V_i and V_j that distance apart. This indicator may be interpreted as a coefficient of intra class correlation between the gene frequencies for all the pairs of villages separated by the same distance. The kinship coefficient is expected to decrease with distance and its estimate may be fitted by a monotonically decreasing function of the type:

$$\psi(x) = \frac{ae^{-bx}}{(1+x)^c}$$

where a is the mean coefficient to kinship for local population (equivalent to the coefficient of inbreeding as a result of subdivision of a population). b is a function of the standard deviation of the distribution of distance between

villages and of the systematic pressure on the genetic marker, and c is a coefficient measuring the dimensionality of migration.

Bechelli concluded that "if we consider that the biological and environmental factors and the socio economic condition in the different villages were fairly uniform, the relation between prevalence rates and the distance between villages would be primarily a function of the number of leprosy and other infectious cases. An untreated Lepromatous patient exposes those in close contact with him to a high risk of infection, and the risk decreases with a decrease in contact".

In a similar study of how the incidence of Leprosy does relate to prevalence, Lechat (1981) observed that if such a quantitative relationship can be established, it could become possible to

- (1) predict future incidences under present conditions of control.
- (2) simulate how changes in the control measures affect incidence.

The mathematical model employed was as follows:

$$(\text{incidence})_t = f(\text{prevalence})_{t-j}$$

where annual incidence is considered as dependent on past prevalence and j corresponds to the duration of the incubation period.

The model was run on a twenty-year time period in order to achieve (1) and (2) above. Of all the control measures he used, the specific vaccination for leprosy comes out by far as the most effective measure. With a 100% vaccine coverage, incidence of new cases was predicted to reduce to zero in 11 years.

He concluded that leprosy cannot bring results overnight. Long term planning and sustained efforts are required. The message is of special importance for international agencies and non-governmental organizations,

which at times display a tendency to expect short term results and get discouraged when the so-called eradication is not soon materializing.

Leprosy is a chronic disease caused by infection with *mycobacterium leprae*. Susceptibility to leprosy is influenced by both genetic and non-genetic factors and the disease is known to cluster in families. One measure of genetic effect is the relative recurrence risk ratio λR . Estimate of this parameter can be inflated if environmental risk factors which also cluster in families, such as household contact, are not properly accounted for. They presented the result of fitting a cross ratio model that allows estimation of the odds ratio of disease conditional on disease or no disease in a given relative, given measured covariates. From the model, they could predict fitted values for λR that represent familiar risk not accounted for by other covariates including observed household contact. If all the covariates could be measured, this would be the "genetic relative risk ratio". They found that $\lambda R > 1$ for all relative pairs except grandparent-grandchild, and $\lambda R > 2$ for siblings Chris Wallage et al (2003).

In a related study Roy (2003) in a letter to the Editor titled "What is the actual male/female sex ratio in Leprosy patients?", stated that during a period of 30 years, carrying out leprosy treatment in North Eastern Nigeria, ending in 1982, they noted a puzzling pattern of male/female ratio in the out patient and inpatient population. A study done in 1969 of 6,691 patients revealed that 74.3% of patients were male. 32.6% female. Thus there is a preponderance of male of 2/3. The conclusion from the study is that leprosy infects men more severely.

Continuous Time Markov process model for the spread of AIDS Epidemic has been discussed Iwunor (2001). A continuous time Markov

Process model with four transient and two absorbing states was developed to be used as a framework for analyzing the spread of AIDS. In the model presented, individuals in a population are classified according to their condition with respect to HIV infection into six states, namely: Murray (1989).

S_1 : Susceptible, S_2 : Infectives, S_3 : Seropositive non-infectives, S_4 : AIDS Patients
 S_5 : Natural (non-AIDS induced) deaths, S_6 : AIDS induced deaths.

States S_1 to S_4 are transient while S_5 and S_6 are absorbing. The paper presented a theoretical result relating to the application of the continuous time Markov process model in studying the spread of AIDS epidemic. The results are expected to have practical usefulness in tracking the spread of this menacing epidemic in situations where the relevant data could be generated.

Several attempts have been made in the past few years at developing models for studying aspects of human reproduction process. Iwunor (2001) in the paper titled "A Semi-Markov Process Model in human reproduction" discussed the application of the Semi-Markov process model in studying the human reproductive process.

The model considered the reproduction pattern of a married female known to be non-pregnant and fecundable at the time of marriage. At any time after marriage (and before the occurrence of menopause or secondary sterility) this woman can be in one, and only one, of the following states with respect to reproductivity.

S_0 = non-pregnant, fecundable state.

S_1 = pregnant state.

S_2 = postpartum sterile period associated with abortion or foetal loss.

S_3 = postpartum sterile period associated with still birth.

S_4 = Postpartum sterile associated with live birth.

It follows that the reproductive history of a female is characterized completely by the knowledge of the sequence in which these states are visited and of the length of time spent in each state at each visit.

Some parameters provided in the model include:

1. The First Passage and re-occurrence times.
2. The Conception rate and Birth rate.
3. The limiting state probabilities.

The model thus provides a very important theoretical framework for understanding the fertility behavior of women by tracking the actual fertility performance of a cohort of women.

The Semi-Markov Process model provides an important tool for assessing the impact of different direct fertility interventions such as Contraceptive use, abortion, breastfeeding, abstinence etc., on fertility reduction. It was observed that the result presented will be of great value to population programme designers and implementers.

Markov and Semi-Markov processes have been applied to manpower system in recent years. Iwunor (2001) in his paper titled "Forecasts of the grade sizes in a manpower system assessed on the Markov and Semi-Markov process models" discussed the forecast of the mean grade sizes in a Markov manpower system with Poisson recruitment based on the Markov and Semi-Markov process models.

In that paper, forecasts of the mean grade sizes for a five-grade universities faculty manpower system are obtained by applying the theories of the continuous time homogeneous Markov process and Semi-Markov process

models with Poisson recruitment . The limiting grade sizes are obtained based on each of the models. The reliability of the forecasts are tested and the relative performance of the two models were compared.

The models considered a five grade faculty manpower system namely: S_1 – Assistant Lecturer, S_2 – Lecturer, S_3 – Senior Lecturer, S_4 – Reader and S_5 – Professor. The absorbing state S_6 is the state of having departed the system. It was assumed that recruitment is allowed into any of the grades and wastage (retirement, resignation, dismissal and death) is possible from any of the grades.

It was concluded that by incorporating information on the length of stay in each grade before moving to the next, a Semi-Markov process model yields better forecast of the mean grade sizes compared with a Markov process model, although, in terms of information requirement and computational ease, the latter model has some merit. A related study by the same author cited in Iwunor (2001) is Iwunor (1987).

In a related study Uche (2001) provided a number of models in his work titled " Stochastic Models in Education and Manpower". The Markovian Model of Graded Systems (Education) considered the hierarchical concept in education, such as the grades of the system, movement between grades in hierarchy, movement within the system and out of the system and partition of grades into absorbing and non-absorbing states.

The models also considered the homogeneous and heterogeneous classes. That is, a class of students may be made of fast movers and slow movers. If transition is considered for this class with the two types of movers lumped together, we have a heterogeneous class. If the fast movers are

separated and treated separately, we have homogenous sub-classes out of the class.

The models further explain the use of the fundamental matrix P in the aspect of educational planning. Such as the probability of going from one grade to another in a given year, the probability that a student in a given grade will still be in the University after a number of years and also the average number of years of schooling left.

Other graded systems discussed are:-

- (1) the models discussed above can be applied to any other graded or hierarchical system, for example a career progressions.
- (2) the Health Sector – for any living organism, the state of being in good health (G), Sick (S) or Death (D). An explanation was offered for the transition between these states, the absorbing state (D) and the expected transition times.

Generally, the models provide a framework for specific research work in any identified area of the graded system. Related studies by the same author have been reported in Uche (1987, 1988, 1991).

2.7 THE MODELLING APPROACH IN THIS PROJECT

The analytical stochastic approach of applied mathematics has been employed in this project. Following Abubakar(1995), the process of leprosy is considered as a semi-Markov process. Four states of the disease were specified. The states are finite, mutually exclusive and exhaustive. The first three states are transient states and the fourth state is an absorbing state and it is the state of death due to leprosy. The effectiveness of treatment on the

interval transition probabilities is the major result obtained from the model. This model was considered for discrete state and discrete time unit.

In this work in addition to the discrete state and time the model incorporates the discrete state and continuous time unit. This will enable us to obtain information about the leprosy patient at any point in time and provide a basis for comparison.

A three state Markov chain model was also considered for catarrh disease with respect to the two seasonal variation in Nigeria. This model also incorporates the discrete state and continuous time which enables us to obtain information about the catarrh patient at any given point in time. These stochastic analyses could be used as a predictive device to study the health status of leprosy and catarrh patients.

Stochastic models have been employed to explain the uncertainties, which are intrinsic features of dynamic economic systems. The central purpose of theories of economic growth is to understand the factors behind long-run growth of economies, and explain differences in growth performances of economies.

Hongliang (2002), discussed the dynamic implications of the stochastic growth and trade model with the savings rate depending on capital-labour ratio and the policy parameters. They extended the trading two-sector economy with uncertainty and analysed the diffusion process for the capital labour ratio, moreover, the crucial boundary conditions of the diffusion process were examined and the steady-state probability distribution of the capital-labour ratio was derived. Some other related studies are contained in Barro et al (1995),

HEK (1999), Gandolfo (1997), Grossman (1996), Jensen et al (1997), Jensen (1999), and Joshi (1998) to mention just a few.

Markov models have been extensively applied to the management of forestry. Acevedo et al (1995) and his colleagues have described and applied a correspondence between two major modeling approaches to forest dynamics: Transition Markovian models and gap models or JABOWA-FORET type simulators. According to them, a transition model can be derived from a gap model by defining states on the basis of species, functional roles, vertical structure or other convenient cover types. A gap-size plot can be assigned to one state according to the dominance of one of these cover types. A semi-Markov framework is used for the transition model by considering not only the transition probabilities among the states but also the holding times in each transition. The holding times are considered to be a combination of distributed and fixed time delays. Extensions in spatial are possible by considering collections of gap-size plots and the proportions of these plots occupied by each state. The advantages of this approach include; reducing simulation time, analytical guidance to the simulations, direct analytical exploration of hypothesis, and the possibilities of fast computation from closed-form solutions and formulae. A preliminary application to the H.J. Andrew forest in the Oregon cascades was presented for demonstration.

In a related application of Markov models, Rajulton (1992) reviewed some types of analysis that are possible using life history information that includes data on the timing, sequence, and a number of occurrences of specific life events; the paper aims at bringing out relevant points regarding two fundamental assumptions in life history analysis (a) that a specific stochastic

process generates events, which can be appropriately analyzed and (b) that certain characteristics of individuals, as well as of context, affect change processes.

The application of Markovian assumptions to the study of the theory of queues has a long history. This gave rise to the classification of Queues generally into the Markovian and non- Markovian Queues. The Markovian queues are the most popular, and are easily handled. Some of the most recent studies in this field include Hiroyuki et al (2003). This paper considers a work conserving FIFO single-server queue with multi batch Markovian arrival streams governed by a continuous time finite-state Markov chain. A particular feature of this queue is that service time distributions of customers may be different for different arrival streams. After briefly discussing the actual waiting time distributions of customers from respective arrival streams, they derived a formula for the vector generating function of the time-average joint queue length distribution in terms of the virtual waiting time distribution. Further assuming the discrete phase-type batch size distributions, they developed a numerically feasible procedure to compute the joint queue length distribution.

Similar work has been reported in Soohan et al (2003) titled Fluid Flow Models and Queues. A connection by stochastic coupling, Guan-lin et al (2003) in the paper β -Invariant measures for transition matrices of GI/M/I type. In another development, a new type of discrete self-composability and its application to continuous-time Markov processes for modeling count data time series, has been reported in Rong et al (2003), and Qi-Ming (2003) has also published a related work he titled, A fixed point approach to the classification of Markov chains with Tree State.

Lawrence (2003) and his colleague in the study titled, Statistical Signal Processing with Nonnegativity Constraints, observed that, Nonnegativity Constraints are frequently in statistical learning and pattern recognition, that, multiplication updates provide natural solutions to optimization involving these constraints. One well known set of multiplicative updates is given by the expectation maximization algorithm for hidden Markov Models, as used in automatic speech recognition. Recently, they derived similar algorithm for nonnegative deconvolution and nonnegative quadratic programming. These algorithms have applications to low-level problems in voice processing, such as the training of large margin classifiers.

In the maximum likelihood estimation, they begin by reviewing multiplicative updates and nonnegativity constraints in a familiar context. Maximum likelihood (ML) estimation in discrete hidden Markov Models (HMMS) also cited in Baum (1972). They considered an HMM with n hidden states $S \in (1, 2, \dots, n)$ and in observations $O \in (1, 2, \dots, m)$. The parameters of the HMM are the transition matrix $a_{ij} = P(S_{t+1} = j | S_t = i)$, the emission matrix $b_{ij} = P(O_t = j | S_t = i)$, and the initial distribution $\pi_k = P(S = k)$. These parameters obey simplex constraints. They are nonnegative, and the distributions they represent must be properly normalised. The goal of ML estimation is to maximize the log-likelihood $L = \log P(a_1, a_2, \dots, a_T)$ of one or more observation sequences.

Specific models used in current research include Markov decision processes, semi-Markov decision processes hidden Markov models, partially observable Markov decision processes; reinforcement learning, in particular hierarchical and memory-based methods. The applications involve complicated

models of learning and sequential decision-making under uncertainty in single-agent and multi-agent domains and their application to real world problems in robotics and industrial processes. These results have been extensively reported in the publications, Ghavamzadeh (2003), Ali (2001) and Ali (1996) respectively.

Similar results have also been presented in the conference papers by the same author in Ghavamzadeh (2003), (2002) and (2001) respectively.

2.8 LEPROSY DISEASE

DEFINITION OF LEPROSY

Many definitions of leprosy exist but Hunter (1966) defined leprosy as a chronic infectious disease primarily of the skin and nerves caused by *Mycobacterium leprae*. It is one of the least infections of all the infectious diseases. The incubation period varies from less than a year to many years, but probably averages three to five years.

TYPES OF LEPROSY

Several variants of the disease are demonstrable, but the disease can be divided generally into two polar types; tuberculoid and lepromatous. A transitional or demorphous type may show a variable degree of similarity to the tuberculoid or the lepromatous types depending upon which pole it approximates.

The non-lepromatous cases exhibit resistance to the infections evidenced by paucity of bacilli in the lesions and their tissue response. In the lepromatous

type there is obvious lack of resistance with an abundance of bacilli in the lesion.

TUBERCULOID

Tuberculoid and the non-lepromatous types have a small number of bacilli limited to the intracellular locations and ordinarily have no means of exit from the body, Job (1981). In other words, this group of leprosy is not responsible for the spread and transmission of leprosy on a large extent.

LEPROMATOUS

Lepromatous types are so baccilliferous to such an extent that organisms overflow from them into the environment. The patients of lepromatous and the borderline lepromatous discharge *Mycobacterium leprae* into the surrounding through Nasal secretions, saliva, exudate from ulcer on the lepromatous skin and the normal secretions of the sweat, and mammary glands, Job, (1981).

The traditional and the simplest explanation of the spread of leprosy is by close and pro-longed contact of the susceptible individual with infectious case. The source of infection is often not known. Susceptibility is important in the understanding of the epidemiology, natural history and clinical classification of leprosy, probably all cases go through an indeterminate phase, whether the point of entry is through the broken or unbroken skin.

DISTRIBUTION

Leprosy is widely distributed in the tropical and sub-tropical regions. This constitutes the top 25 countries that have nearly 94% of the world cases, Noordeen et al (1992). From the mid-sixties to the mid-eighties global estimates appeared to be constant at between 10 and 12 million. The

introduction of multi-drug therapy (MDT) in many countries and the consequent reduction of prevalence of the disease has necessitated a re-assessment of the global estimate. Based on the available data and its interpretation, the number of leprosy cases in the world in 1991 had been estimated at 5.5 million. The number of individuals with deformity due to leprosy had been estimated as between 2 and 3 million. The following table summarizes the regional distribution of leprosy cases.

Table 1: The estimated and Registered cases of Leprosy in the (WHO) regions 1991 (×1,000)

| REGION | ESTIMATED | REGISTERED |
|--------------------------|-----------|------------|
| 1. Africa | 735 | 280 |
| 2. South East Asia | 3,744 | 2,273 |
| 3. America | 327 | 295 |
| 4. East Mediterranean | 152 | 57 |
| 5. West Pacific | 207 | 89 |
| Total (top 25 countries) | 5,165 | 2,994 |
| Total (all countries) | 5.511 | 3,162 |

Source: Noorden (1992)

The top 25 countries have the largest number of estimated leprosy cases and contributes 93.7% of the total estimated cases in the world.

DIAGNOSIS AND TREATMENT

Diagnosis

The cardinal diagnostic signs are the presence of anaesthetic macular lesion or thickening and tenderness of peripheral nerve trunks and the demonstration of bacilli. Search should be made for suspicious macules or infiltrations of the skin and for the thickening of ear lobes and the eye brows. The peripheral nerves should be palpated carefully. The patient should be examined in bright sunlight to appreciate fully even to find certain lesions of leprosy.

Smears should be made from several sites, skin lesion, earlobes and the nasal septum. Since bacilli are usually obtainable only from lepromatous and the demorphous lesions, many cases should be diagnosed on the basis of clinical appearance and the presence of anaesthesia in simple macular or tuberculoid lesion. In such lesions, loss of sensitivity to light touch and absence of pain on pin prick justify the diagnosis. Test for instamine flare and for sweating afford Confirmatory evidence.

TREATMENT

General treatment, including personal and environmental hygiene, a well balanced diet and the correction of concomitant conditions is important. With such measures even severe lepromatous cases may show some degree of amelioration, at least for a time, Hunter (1966).

Ideally, the most promising drugs for use in combination with dapsone or for the treatment of patients with dapsone resistant leprosy are: Rifampicin, clofazimine, ethionomide, prothionamide and thiacethazone, Ellard (1981).

DURATION OF TREATMENT

Dapsone treatment of paucibacillary leprosy is still of long duration; 2 - 5 years. Lowe recommended 24 months treatment, Wheate and Pearson suggested 2 years to 5 years and the third and fourth WHO expert Committee reports recommended that tuberculoid patients should continue treatment for 18 months after all activities has ceased and the lesions have become quiescent, which means a total of 24 - 36 months (See Warndorff, 1982).

It was observed that Rifampicin (RMP) is highly bactericidal for mycobacterium leprae, Warndorff (1982). Based on previous studies it was thought that it should be possible to cure patients with short regimen of 8 weekly doses of 900 mg Rifampicin. Nevertheless, treatment of paucibacillary leprosy should be aimed at two objectives. The killing of bacilli and stopping the allergic reaction. Evidently, Rifampicin can realise the first objective rapidly and efficiently, since in the present series, no relapses were observed after 8 weekly doses of 900 mg of Rifampicin. The second objective will have to be taken care of by other drugs.

RELAPSE RATE

For a long term treatment with dapsone, several cases of relapse had been reported. A follow up study of 6 months to 4 years on 69 patients observed 11.6% relapses, Lowe (1954) cited in Waaldttk (1989). Seven of the eight relapses occurred within 3 - 12 months after treatment ceased and one at 28 months. Three of the 7 patients had been treated for less than a year, 3 for between 1. and 2 years and 2 for 2 - 2.5 years.

NATURAL HISTORY OF LEPROSY

Leprosy is a common disease that may begin at any age but due to long incubation period of *Mycobacterium leprae* (2 - 5 years), its appearance during infancy and childhood is minimal. For the greater part of leprosy patients, there is a history of leprosy in members of the immediate family. Perhaps, this is the reason why some people think that leprosy is hereditary.

There is no spontaneous recovery without treatment and usually all latent cases develop overt disease except if dying in the meantime. Resistance to leprosy is not uncommon be it genetic or immunological.

It is generally accepted that *Mycobacterium leprae* (Hansen, 1874), cited in Hunter (1966) is the etiological agent of leprosy. Deformities in fingers, feet (toes), eye brows, nose and earlobes is not uncommon with leprosy patients. Death due to leprosy itself is infrequent. Pulmonary tuberculosis and nephritis are common terminal events, although the frequency of tuberculosis has greatly diminished since the advent of sulfone treatment, Hunter (1966).

2.9 CATARRH DISEASE

Catarrh otherwise known as common cold 'Oterion Anoma catarrhdic Rhinitis', is caused by the influenza virus. The incubation period is from 24 hours to 48 hours. It is an air-borne disease resulting from breathing in infected air through the nostril tube. This develops into the inflammation of a mucus membrane usually accompanied by excess secretion of mucus.

Other types of catarrh are hay fever, bronchial catarrh, gastric and intestinal and vesical catarrh, the inflammation of the bladder. The catarrh of interest in this paper is the one in which the mucus membrane is at first

congested swollen, hot and dry and then subsequently produces a free mucoid or watery discharge , which may become purulent before drying up as the inflammation abates.

TREATMENT

The treatment involves the application of Nasal decongestants (Ollivirin Nospamin) and Prolachic antibiotic (septrin) in addition to analgesic (paracetamol).

2.10 THE SEASONAL VARIATIONS IN NIGERIA

Generally, two seasonal variations can be identified in Nigeria. The wet seasons wind and rainfall (April to October); the full effect of the tropical maritime air mass as the main factors which bring rainfall is felt in this season. Dry season wind and rainfall (November to March). This is the dry season when rainfall is least.

The mathematical formulations on the epidemiology of leprosy are not new. These in several occasions have been used to study the transmission and spread of the disease side by side with the past prevalence and incidence of new cases. Leprosy is the least infectious of all the contagious diseases. The cases of leprosy may be found anywhere in the world but much more in the tropical and subtropical countries. The disease is not hereditary as some people may want to believe and Leprosy patients can be treated and cured. The model developed in this project incorporates uncertainty and variability.

CHAPTER THREE

3.0 STOCHASTIC PROCESSES, FORMAL DEFINITIONS AND THEORY

3.1 STOCHASTIC PROCESSES

The family of random variables $\{X(t), t \geq 0\}$ indexed by the time parameter t . The values assumed by the process are called 'states' and the set of possible values are called the state space. The set of possible values of the indexing parameter is called the 'parameter space' which can be either continuous or discrete. In the discrete case, the process is represented as $\{X_n, n=0, 1, 2, \dots\}$.

3.2 MARKOV PROCESSES

The stochastic process occurring in most real-life situations are such that for a discrete set of parameters $t_1, t_2, \dots, t_n, t, T$, the random variables $X(t_1), X(t_2), \dots, X(t_n)$ exhibit some sort of dependence. The simplest type of dependence is the first-order dependence underlying the stochastic process. This is called Markov dependence, which may be defined as follows;

Consider a finite (or countably infinite) set of points $(t_0, t_1, \dots, t_n, t)$, $t_0 < t_1 < t_2 < \dots < t_n < t$ and $t, t_r \in T$ ($r = 1, 2, \dots, n$) where T is the parameter space of the process $\{X(t)\}$. The dependence exhibited by the process $\{X(t)\}$, $t \in T$ is called "Markov - dependence" if the conditional distribution of $X(t)$ for given values of $X(t_1), X(t_2), \dots, X(t_n)$ depends only on $X(t_n)$ which is the most recent known value of the process.

that is, if

$$\begin{aligned} P[X(t) \leq x \mid x(t_n) = x_n, x(t_{n-1}) = x_{n-1}, \dots, x(t_0) = x_0] \\ &= P[x(t) \leq x \mid x(t_n) = x_n] \\ &= F(x_n, x; t_n, t) \end{aligned} \tag{1.0}$$

The stochastic process exhibiting this property is called a 'Markov Process'. In a Markov process, therefore, if the state is known for any specific value of the time parameter t , that information is sufficient to predict the next behavior of the process beyond that point.

As a consequence of the property given by (1.0), we have the following relation:

$$F(x_0, x; t_0, t) = \int_{y \in S} F(y, x, \tau, t) dF(x_0, y, t_0, \tau) \quad (1.1)$$

where $t_0 < \tau < t$ and S is the state space of the process $x(t)$.

When the stochastic process has a discrete state space and a discrete parameter space, (1.0) and (1.1) take the following forms: for $n > n_1 > n_2 > \dots > n_k$ and n and n_1, n_2, \dots, n_k belonging to the parameter space.

$$\begin{aligned} p(X_n = j | X_{n_1} = i_1, X_{n_2} = i_2, \dots, X_{n_k} = i_k) \\ = p(X_n = j | X_{n_1} = i_1) \\ = p_{ij}(n_i, n) \end{aligned} \quad (1.2)$$

Using this property, for $m < r < n$ we get

$$\begin{aligned} P_{ij}^{(m, n)} &= P(x_n = j | x_m = i) \\ &= \sum_{k \in S} P(x_n = j | x_r = k) P(x_r = k | x_m = i) \\ &= \sum_{k \in S} P_{ik}^{(m, r)} P_{kj}^{(r, n)} \end{aligned} \quad (1.3)$$

where we have again used S as the state space of the process.

Equations (1.1) and (1.3) are called the "Chapman-Kolmogorov equations" for the process. These are basic equations in the study of Markov processes. They enable us to build a convenient relationship for the transition

probabilities between any points in T at which the process exhibits the property of Markov – dependence.

Another statement of the Chapman – Kolmogorov equation and the proof is given below:

$$\begin{aligned}
 P_{ij}(t+s) &= P(X(t+S) = j | X(0) = i) \quad (\text{definition}) \\
 &= \sum_k P(X(t+S) = j, X(t) = k | X(0) = i) \quad (\text{marginal from joint}) \\
 &= \sum_k P(X(t+S) = j | X(t) = k, X(0) = i) P(X(t) = k | X(0) = i) \\
 &= \sum_k P(X(t+S) = j | X(t) = k) P(X(t) = k | X(0) = i) \quad (\text{Markov assumption}) \\
 &= \sum_k P(X(s) = j | X(0) = k) P(X(t) = k | X(0) = i) \quad (\text{Stationarity}) \\
 &= \sum_k P_{kj}^{(s)} P_{ik}^{(t)} \quad (\text{definition})
 \end{aligned}$$

Thus $P_{ij}(t+s) = \sum_k P_{ik}^{(t)} P_{kj}^{(s)}$

This is the Chapman-Kolmogorov equation in general form

We shall use it in the special form of

$$P_{ij}(t + \Delta t) = \sum_k P_{ik}^{(t)} P_{kj}(\Delta t)$$

This equation requires the Markov assumption to permit a multiplication of the probabilities referring to events during t and to events during Δt . it also requires stationarity to permit use of the same probability functions for the interval t and for the later interval Δt .

Depending on the nature of the state space and the parameter space, we can divide Markov processes into four classes, which are given here in the form of a table. Wherever the parameter and state spaces are discrete the Markov process is called Markov chain. Otherwise the process is simply referred to as a Markov process.

Table 2: Classification of Markov processes

| PARAMETER SPACE | STATE SPACE | |
|-----------------|----------------|----------------|
| | Discrete | Continuous |
| Discrete | Markov Chain | Markov Process |
| Continuous | Markov Process | Markov Process |

3.3 MARKOV CHAINS

A Markov chain is the Markov process with discrete time and parameter spaces whose state space could be finite or countably infinite.

Let $\{X_n, n = 0, 1, 2, \dots\}$ be a Markov chain with a state space

$S \subseteq Y = \{0, 1, 2, \dots\}$. While discussing a finite m-state chain, we shall identify the state space S to be given by the set $\{1, 2, \dots, m\}$. The element P_{ij} , means the probability that $x_1 = j$ if you know that $x_0 = i$. It is a conditional probability

$$P_{ij} = p(X_1=j|X_0=i).$$

In the time homogeneous Markov chain the n - step transition probabilities are defined $p_{ij}^{(n)} = p(X_n=j|(X_0=i)$

The conditional probability $P(X_n=j|X_{n-1}=i)$ is referred to as the one step transition probability from i to j at time n. If for all m and n,

$P(X_n=j|X_{n-1}=i) = P(X_m=j|X_{m-1}=i)$, the Markov chain is said to be stationary.

Stationary and time homogeneous are synonymous.

The stationary assumption is one of 'constancy' over time. It suggests stability of the process, although, of course, it does not imply that the process remains in fixed state or even that there is a sluggishness in the rate at which transition occurs. It is the probability mechanism that is assumed stable.

'n-step' refers to the time interval between observations. In matrix form,

$$P = [P_{ij}] = \begin{bmatrix} P_{00} & P_{01} & P_{02} \dots \\ P_{10} & P_{11} & P_{12} \dots \\ \vdots & \vdots & \vdots \end{bmatrix}$$

and

$$P^{(n)} = [P_{ij}^{(n)}] = \begin{bmatrix} P_{00}^{(n)} & P_{01}^{(n)} & P_{02}^{(n)} \dots \\ P_{10}^{(n)} & P_{11}^{(n)} & P_{12}^{(n)} \dots \\ \vdots & \vdots & \vdots \end{bmatrix}$$

we have $\sum_{j \in S} P_{ij}^{(n)} = 1$

3.4 THE n- STEP TRANSITION PROBABILITY MATRIX

Let P be the transition probability matrix of a Markov chain and let $P_j^{(n)}$ be the probability that the process is in state j after n transitions (unconditional probability), denoted by the row vector of probabilities $P_j^{(n)}, j \in S$.

The n -step transition probabilities $P_{ij}^{(n)}$ and the unconditional probabilities $P_j^{(n)}, i, j, \in S$ are determined by the following.

Theorem 3.1 $P^{(n)} = P^n$ 1.4

and $P^{(n)} = P^{(0)}P^n$ 1.5

For the proof, see Bhat (1984) pages 38 and 39.

3.5 FIRST – PASSAGE AND RETURN PROBABILITIES

The probabilities treated so far answer questions of the general form that is, what is the probability of being in a certain state at a time? One other important question of interest is how long will it take to reach a certain state? The answer involves probabilities, but the random variable is the number of transitions that occur before a specified state is reached rather than the state after a specified number of transitions.

When we speak of the number of steps required to reach state j for the first time, we mean the number of steps required to reach state j for the very first time.

Definition (1):- A state i is said to be recurrent if and only if starting from state i , eventual return to this state is certain. In terms of probabilities f_{ii} , this implies that the state i is recurrent if and only if $f_{ii} = 1$

A recurrent state can be further classified either as null recurrent or positive recurrent.

- (1) A recurrent state i is said to be null recurrent if, and only if, the mean recurrence time is ∞ , that is, if $m_{ii} = \infty$
- (2) A recurrent state is said to be positive recurrent if, and only, if the mean recurrent time is finite, that is, $m_{ii} < \infty$

For a finite Markov chain m_i , $i \in \mathcal{S}$ is always finite. Therefore null recurrence is possible only when the state space is countably infinite.

We therefore consider the first passage probability $f_{ij}^{(n)}$ defined thus ;

$$f_{ij}^{(n)} = P(x_n = j, x_{n-1} \neq j, x_{n-2} \neq j, \dots, x_1 \neq j | x_0 = i)$$

$$= P_{ij}^{(n)} - \sum_{k=i}^{n-1} f_{ij}^{(k)} P_{jj}^{(n-k)}$$

Hence the $f_{ij}^{(n)}$ can be obtained iteratively if the $P_{ij}^{(n)}$ are known clearly
 $f_{ij}^{(1)} = P_{ij}$.

The above definition assumes that i and j are distinct. If they are not, the formal definition would be exactly the same but we would speak of 'first return' rather than first passage so that

$$f_{ii}^{(n)} = P(x_n = i, x_{n-1} \neq i, x_{n-2} \neq i, \dots, x_1 \neq i | x_0 = i)$$

3.6 ERGODIC MARKOV CHAINS

When the process is irreducible, recurrent-positive and aperiodic, (see definitions 1,3, and 6). We call the Markov chain ergodic. When the model is ergodic, several additional quantities, other than the transition probabilities can easily be calculated. Two of the most important of these are steady-state probabilities and mean first passage times.

Mathematically, $P^{(n)}$ and $P^{(n+1)}$ are essentially the same for large n ,

$$P^{(n)} = P^{(n+1)} P$$

And

$$\lim_{n \rightarrow \infty} P^{(n)} = \lim_{n \rightarrow \infty} P^{(n+1)} P$$

$$\begin{bmatrix} \pi_1 & \pi_2 & \pi_3 & \cdots \\ \pi_1 & \pi_2 & \pi_3 & \cdots \\ \vdots & \vdots & \vdots & \vdots \end{bmatrix} = \begin{bmatrix} \pi_1 & \pi_2 & \pi_3 & \cdots \\ \pi_1 & \pi_2 & \pi_3 & \cdots \\ \vdots & \vdots & \vdots & \vdots \end{bmatrix} P$$

$$\pi = \pi P$$

Let N_{ij} represent the random variable for the number of Epoch to reach j for the first time starting from i , then

$$P(N_{ij} = n) = f_{ij}^{(n)}$$

Because the $f_{ij}^{(n)}$ give the distribution of N_{ij} , the passage time from i to j , denoted m_{ij} is given by

$$m_{ij} = E(N_{ij}) = \sum_{n=1}^{\infty} n f_{ij}^{(n)}$$

In this case $i = j$, M_{ij} would be called the mean recurrence time.

3.7 MARKOV CHAINS AND CLASSIFICATION OF STATES

The value of x_n for a specific realization of the process is called the state of the process.

Definition (2): State j is said to be accessible from state i if j can be reached from i in a finite number of steps. If two states i and j are accessible to each other, then they are said to communicate. Probabilistically, these definitions imply

$$i \rightarrow j \text{ (} j \text{ accessible from } i \text{) if for some } n \geq 0 \quad P_{ij}^{(n)} > 0$$

$$j \rightarrow i \text{ (} i \text{ accessible from } j \text{) if for some } n \geq 0 \quad P_{ji}^{(n)} > 0$$

$$i \leftrightarrow j \text{ (} i \text{ and } j \text{ communicate) if for some } n \geq 0 \quad P_{ij}^{(n)} > 0$$

$$\text{and for some } m \geq 0 \quad P_{ji}^{(m)} > 0$$

Conversely,

$$i \nrightarrow j \text{ (} j \text{ is not accessible from } i \text{) if for all } n \geq 0 \quad P_{ij}^{(n)} = 0$$

$$j \nrightarrow i \text{ (} i \text{ is not accessible from } j \text{) if for all } n \geq 0 \quad P_{ji}^{(n)} = 0$$

$$i \nleftrightarrow j \text{ (} i \text{ and } j \text{ do not communicate) if for all } n \geq 0 \quad P_{ij}^{(n)} = P_{ji}^{(n)} = 0$$

It has been shown Bhat(1984) that all the states that communicate in a finite Markov chain form an equivalence relation.

Definition (3): If a Markov chain has all its states belonging to one equivalence class, it is said to be irreducible.

Definition (4): A state i is said to be transient if, and only, if starting from state, there is a positive probability that the process may not eventually return to this state. This implies that $f_{ii}^* < 1$

Definition (5): A state i is said to be an absorbing state if and only if $P_{ii} = 1$.

When i is absorbing $f_{ii}^{(1)} = P_{ii} = 1$ and hence $f_{ii}^* = 1$ and $m_i = 1$, showing that i is positive recurrent.

Definition (6): The period of a state i is defined as the greatest common divisor of all integers $n \geq 1$, for which $P_{ii}^{(n)} > 0$. When the period is 1, the state is referred to as aperiodic.

3.8 DISCRETE STATE AND CONTINUOUS TIME PROCESSES

A continuous time stochastic process is similar in many respects to a discrete time stochastic process. However, complexity does occur because each infinitesimal time is available as a possible transition time.

A continuous time stochastic process $\{x(t)\}$ is an infinite family of random variables indexed by the continuous real variable t . That is, for any fixed t , $x(t)$ is a random variable, and the collection of all of these (for all t) is the stochastic process.

We think of t as time, so we may expect $x(t_1)$, the random variable at time t_1 to be dependent on $x(t_0)$, where $t_0 < t_1$ but not upon $x(t_2)$, where $t_2 > t_1$.

We refer to the value of $x(t_1)$ as the state of the process at time t_1 . we assume $x(t)$ are discrete – state, continuous – time stochastic processes.

If for all t_n, t_{n-1}, \dots, t_0 satisfying $t_n > t_{n-1} > \dots > t_0$, we have that $P(x(t_n) = j_n | x(t_{n-1}) = j_{n-1}, \dots, x(t_0) = j_0) = P(x(t_n) = j_n | x(t_{n-1}) = j_{n-1})$ we say that the process has the Markov property or is a (continuous time) Markov process.

Definition (7): A Markov process is said to be time homogeneous or stationary if

$$P(x(t_2) = j | x(t_1) = i) = P(x(t_2 - t_1) = j | x(0) = i).$$

For all i , all j , all t_1 and t_2 such that $t_1 < t_2$.

In words, the process is stationary if these conditional probabilities depend only on the interval between the events rather than on absolute time.

A stationary Markov process is completely described by its transition probability functions, denoted $P_{ij}(t)$ where $P_{ij}(t) = P(x(t) = j | x(0) = i)$

Note: $P_{ij}(t)$ functions are probabilities, for all t . they are non negative, bounded functions because they must lie between 0 and 1.

$P_{ij}(0) = P(x(0) = j | x(0) = i)$. Clearly, for i different from j ,

$P_{ij}(0) = 0$ and for i equal to j , $P_{ij}(0) = 1$. if we fix i and vary j over all states, the sum of the $P_{ij}(t)$ must equal 1 (for all t).

$$\begin{aligned} \sum_j P_{ij}(t) &= \sum_j P(x(t) = j | x(0) = i) \\ &= P(x(t) = \text{any of its possible states} | x(0) = i) \\ &= 1 \end{aligned}$$

Under the assumption that the $P_{ij}(t)$ are continuous functions of time, we can express P_{ij} for small Δt by the use of Maclaurin 's series.

$$P_{ij}(\Delta t) = P_{ij}(0) + P'_{ij}(0) \Delta t + O(\Delta t)^2$$

Where $O(\Delta t)^2$ represents all terms of the order of $(\Delta t)^2$ or higher. If we consider this expression for $i \neq j$, and

let $\lambda_{ij} = P'_{ij}(0)$, we obtain

$$P_{ij}(\Delta t) = \lambda_{ij} \Delta t + O(\Delta t)^2$$

We may think of this as a linear approximation to $P_{ij}(t)$ which is a good approximation as long as Δt is small

The λ_{ij} is called the transition rate from i to j .

Since $P_{ij}(0) = 0$ and this is the minimum value, we should be certain that λ_{ij} is non negative.

For $i = j$, the Maclaurin's series expansion yields

$$P_{jj}(\Delta t) = 1 + P'_{jj}(0) \Delta t + O(\Delta t)^2.$$

And if let $\lambda_{jj} = P'_{jj}(0)$, we get the linear approximation

$$P_{jj}(\Delta t) = 1 + \lambda_{jj}\Delta t + O(\Delta t)^2$$

Since we know that $P'_{ij}(0) = 1$ and that is the maximum value, we may be certain that λ_{ij} is non - positive.

If we now consider the Chapman - Kolmogorov equation

$$P_{ij}(t + \Delta t) = \sum P_{ik}^{(t)} P_{kj}^{(\Delta t)}$$

For small Δt , and substituting linear approximation, we get

$$P_{ij}(t + \Delta t) = P_{ij}^{(t)} [1 + \lambda_{ij}\Delta t + O(\Delta t)^2] + \sum_{k \neq j} P_{ik}^{(t)} [\lambda_{kj}\Delta t + O(\Delta t)^2]$$

and

$$\frac{P_{ij}(t + \Delta t) - P_{ij}(t)}{\Delta t} = P_{ij}(t)\lambda_{ij} + \frac{P_{ij}(t)O(\Delta t)^2}{\Delta t} + \sum_{k \neq j} \left[P_{ik}(t)\lambda_{kj} + \frac{P_{ik}(t)O(\Delta t)^2}{\Delta t} \right]$$

$$= \sum_k P_{ik}(t) \lambda_{kj} + \sum_k \frac{P_{ik}(t) O(\Delta t)^2}{\Delta t}$$

Taking the limit as $\Delta t \rightarrow 0$

$$\frac{dP_{ij}(t)}{dt} = \sum_k P_{ik}(t) \lambda_{kj}$$

The terms of the order (large order) $(\Delta t)^2$ go to zero faster than Δt so these terms drop out.

The result is an exact (not approximate) differential equation for $P_{ij}(t)$ in terms of the $P_{ik}(t)$. It is a linear, first-order differential equation with constant coefficients λ_{kj} 's.

Recognising the above sum as matrix multiplication, we may express all of the differential equations at once in the matrix form

$$\frac{dP(t)}{dt} = P(t)A$$

Where $dP(t)/dt$ is the matrix whose (i,j) th element is $dP_{ij}(t)/dt$, $P(t)$ is the matrix whose (i,j) th element is $P_{ij}(t)$, and A is the matrix whose (i,j) th element is λ_{ij} .

The elements of A may be further related by extending the properties of $P(t)$.

In particular, since for each i

$$\sum_j P_{ij}(t) = 1$$

$$\text{then } \frac{d}{dt} \left[\sum_j P_{ij}(t) \right] \Big|_{t=0} = \frac{d}{dt} [1] \Big|_{t=0}$$

$$\sum_j \frac{d}{dt} P_{ij}(t) \Big|_{t=0} = 0$$

$$\sum_j \lambda_{ij} = 0$$

In words, each row of A must sum to zero. Since every off-diagonal element is non negative, the diagonal element λ_{ii} , must be equal in magnitude and opposite in sign to the sum of others in the same rows. That is,

$$\lambda_{ii} = - \sum_{j \neq i} \lambda_{ij}$$

3.9 SEMI - MARKOV PROCESSES

A semi - Markov process is a process in which changes of state occur according to a Markov chain and for which the time interval between two successive transitions is a random variable whose distribution may depend on the state from which the transition takes place.

Proposition (1): Let $\{X_n, n = 0, 1, \dots\}$ constitute a Markov chain with state space E and transition probability matrix $P = (P_{jk})$. A continuous parameter process $Y(t)$ with state space E defined by $Y(t) = X_n$ on $t_n \leq t \leq t_{n+1}$

is called a semi - Markov process. The Markov chain $\{X_n\}$ is said to be an embedded Markov chain of the semi - Markov process. X_n refers to the state of the process at transition occurring at epoch X_n and $Y(t)$ that of the process at its most recent transition.

WAITING TIME

Let the time spent by the process in state j before its next transition, given that the next transition is state K be a random variable T_{jk} having distribution function

$$W_{jk}(t) = P [T_{jk} \leq t] = P (t_{n+1} - t_n \leq t \mid X_n = j, X_{n+1} = K) \quad j, K = 1, 2, \dots, m.$$

The random variable T_{jk} is called the Surjourn time or waiting depends on the state X_n being visited and the state X_{n+1} to be entered in the very next transition.

INTERVAL TRANSITION PROBABILITY

Theorem(3.2): for all i, j and for $t \geq 0$

$$\phi_{ij}(t) = \delta_{ij} h_i(t) + \sum_K P_{Kj} \int_0^t f_{ik}(x) \phi_{kj}(t-x) dx$$

$$\begin{aligned} \text{where } h_i(t) &= 1 - \sum_k \phi_{ik}(t) \\ &= 1 - W_i(t) \\ &= P(T_i > t) \end{aligned}$$

and $\delta_{ij} = \begin{cases} 0 & i \neq j \\ 1 & i = j \end{cases}$ is the Kronecker's delta function.

In summary, suppose that a process can be in any one of N states $1, 2, \dots, N$ and that each time it enters state i , it remains there for a random amount of time having mean M_i and then makes a transition into state j with probability P_{ij} . Such a process is called a semi - Markov process. We note that if the amount of time that the process spends in each state before making a transition is

identically 1, then the semi – Markov process is just a Markov chain. Thus a Markov process is a semi – Markov process but the converse is not true.

3.10 THE EXPONENTIAL AND THE WEIBULL DISTRIBUTIONS

We shall briefly discuss the exponential and the Weibull distributions as they relate to the duration of stay in a disease state. They have been used in this project for distributions of holding times in states. We end the discussion with some comparisons of the two distribution functions.

3.11 THE EXPONENTIAL DISTRIBUTION

The probability density function of the random variable T having the exponential distribution is given by

$$f(t) = \begin{cases} \lambda e^{-\lambda t} & t \geq 0 \\ 0 & \text{elsewhere} \end{cases}$$

Where $\lambda > 0$

The distribution has λ as a parameter. λ also determines the shape of the distribution. The mean μ of the exponential distribution is

$$\mu = E(T) = \int_{-\infty}^{\infty} t \lambda e^{-\lambda t} dt = \int_0^{\infty} t \lambda e^{-\lambda t} dt$$

Substituting $w = \lambda t \Rightarrow t = w/\lambda$ and $dw = \lambda dt$ in the integrand gives

$$\begin{aligned} \mu &= \int_0^{\infty} \frac{w}{\lambda} e^{-w} dw = \frac{w}{\lambda} e^{-w} \Big|_0^{\infty} - \int_0^{\infty} e^{-w} dw \\ &= \frac{1}{\lambda} \end{aligned}$$

Thus $\mu = 1/\lambda$

$$E(T^2) = \int_0^{\infty} t^2 \lambda e^{-\lambda t} dt$$

Let $w = \lambda t \Rightarrow t = w/\lambda$ and $dw = \lambda dt$

$$\text{So that } E(T^2) = \int_0^{\infty} t^2 \lambda e^{-\lambda t} dt = \int_0^{\infty} \frac{w^2}{\lambda} e^{-w} dw$$

$$\begin{aligned} &= \frac{w^2}{\lambda} e^{-w} \Big|_0^{\infty} - \frac{2}{\lambda} \int_0^{\infty} w e^{-w} dw \\ &= -\frac{2}{\lambda} e^{-w} \Big|_0^{\infty} = \frac{2}{\lambda^2} \end{aligned}$$

The variance σ^2 of the exponential distribution is therefore given by

$$\begin{aligned} \sigma^2 &= \sigma E(T^2) - (E(T))^2 \\ &= 2/\lambda^2 - 1/\lambda^2 = 1/\lambda^2 \end{aligned}$$

$$\text{Thus } \sigma^2 = 1/\lambda^2$$

Definition (7): The survivor function $S(t)$ is given by

$$S(t) = P(T > t)$$

and it is the probability that an individual has survived up to time t .

Suppose $F(t)$ is the distribution function of the random variable T . Then

$$S(t) = 1 - F(t)$$

For the exponential distribution

$$\begin{aligned} F(t) &= P(T \leq t) = \int_0^t f(s) ds \\ &= \int_0^t \lambda e^{-\lambda s} ds \\ &= 1 - e^{-\lambda t} \end{aligned}$$

Therefore

$$S(t) = e^{-\lambda t}$$

To interpret $h(t)$ we consider the conditional probability $P(t < T < t + \Delta t \mid T > t)$. That is, the probability that the individual will die during the next Δt time units, given that he survived at time t . Using the definition of conditional probability, we have

$$\begin{aligned}
 P(t < T < t + \Delta t \mid T > t) &= \frac{P(t < T < t + \Delta t)}{P(T > t)} \\
 &= \frac{\int_t^{t+\Delta t} f(s) ds}{p(T > t)} \\
 &= \frac{\Delta t f(\xi)}{s(t)}
 \end{aligned}$$

Where $t < \xi < t + \Delta t$

The failure rate or the hazard rate, ' h ' associated with the random variable T is given by

$$h(t) = f(t)/S(t)$$

This failure rate is a constant in the case of the exponential distribution.

That is, the hazard rate is given by $h(t) = \lambda$

PARAMETER ESTIMATION

It is clear that the exponential distribution has a simple probability density function. It is specified by a single parameter λ . This parameter is estimated by specifying the mean of the distribution. Thus if the mean μ is specified then the parameter is estimated using

$$\lambda = 1/\mu$$

ILLUSTRATION

The mean holding time μ_{12} in the state of treatment (State 1) see page 104, is 3 years. If the holding time in the state follows the exponential distribution, then the parameter λ is estimated thus:-

$$\lambda = 1/\mu = 1/3 = 0.33 \quad (\text{corrected to 2 dp}).$$

$$\text{Hence } f(t) = \lambda e^{-\lambda t} = 0.33e^{-0.33t}$$

This is illustrated in figure 1.

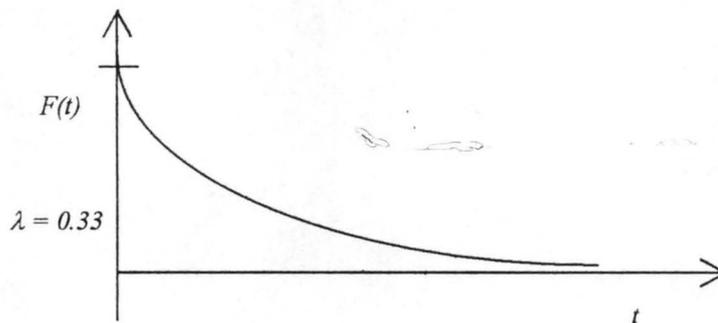


Figure 1: The graph of an exponential distribution.

The exponential distribution is a prominent statistical measurement model. It has the advantage of being specified by one parameter. Most applications are based on its 'memoryless' property, when the measurement variable T has a time dimension. This property refers to the phenomenon in which the history of the past events does not influence the probability of occurrence or future events/present events. The application of the exponential model arises in the theory of queues in conjunction with the Poisson and Erlang models. From the waiting time interpretation of Erlang variable T , it follows that $f(t) = \lambda e^{-\lambda t}$ is the waiting time model to the first Poisson event. But the exponential model is 'memoryless' as mentioned earlier. Consequently, the waiting time to the first Poisson event is the same random variable as the waiting time between any

two adjoining Poisson events. The exponential distribution is a special case of both the Gamma and the Weibull distributions.

Despite the above advantages of the exponential distribution, it has the weakness of the measure of hazard rate which is constant. Thus it does not accurately define the holding time in the states of a disease which changes with time.

3.12 THE WEIBULL DISTRIBUTION

The probability density function of a random variable T having the three parameter Weibull distribution is given by

$$f(t) = \begin{cases} \frac{\beta}{\alpha} \left(\frac{t-c}{\alpha}\right)^{\beta-1} \exp\left[-\left(\frac{t-c}{\alpha}\right)^\beta\right] & t \geq c \\ 0 & t < c \end{cases}$$

$$\alpha, \beta, c > 0$$

The scale parameter is α . It is the characteristic life that specifies the 100 $(1 - e^{-1})^{\text{th}}$ distribution percentile of $(t - c)$. The parameter β determines the shape of the distribution and it is therefore called the 'shape parameter'. The 'location parameter' is c , it shows the position along the t -axis where the distribution should lie. It is also called the threshold parameter, because, if c is the failure time, the probability of failure before time c is zero.

We can always reduce the distribution to a two parameter Weibull by putting $t^1 = t - c$, thus

$$f(t^1) = \begin{cases} \frac{\beta}{\alpha} \left(\frac{t^1}{\alpha}\right)^{\beta-1} \exp\left[-\left(\frac{t^1}{\alpha}\right)^\beta\right] \\ \alpha, \beta > 0 \end{cases}$$

The distribution function is given by

$$F(t) = 1 - \exp\left(-\left(\frac{t}{\alpha}\right)^\beta\right)$$

The mean μ of the two - parameter Weibull distribution is given as

$$\mu = E(T) = \int_0^\infty t f(t) dt = \int_0^\infty t \frac{\beta}{\alpha} \left(\frac{t}{\alpha}\right)^{\beta-1} \exp\left(-\left(\frac{t}{\alpha}\right)^\beta\right) dt$$

Substituting $w = (t/\alpha)^\beta$ then $dw = \beta/\alpha(t/\alpha)^{\beta-1} dt$

so that

$$\begin{aligned} \mu &= \int_0^\infty \alpha w^{\frac{1}{\beta}} \exp(-w) dw \\ &= \alpha \int_0^\infty w^{(1+1/\beta)-1} \exp(-w) dw \\ &= \alpha \Gamma(1+1/\beta) \end{aligned} \tag{3.2}$$

Where Γ denotes the Gamma function. By definition $\Gamma(\alpha) = (\alpha-1)!$

The variance of the two parameter Weibull distribution is given by

$$E(T^2) - (E(T))^2$$

but

$$E(T^2) = \int_0^\infty t^2 \frac{\beta}{\alpha} \left(\frac{t}{\alpha}\right)^{\beta-1} \exp\left(-\left(\frac{t}{\alpha}\right)^\beta\right) dt$$

Put $(t/\alpha)^\beta = w$ then $dw = \beta/\alpha(t/\alpha)^{\beta-1} dt$ and $t = \alpha w^{1/\beta}$

In the integrand gives

$$\begin{aligned} E(T^2) &= \int_0^\infty \alpha^2 w^{\frac{2}{\beta}} e^{-w} dw \\ &= \alpha^2 \int_0^\infty w^{(1+2/\beta)-1} e^{-w} dw \\ &= \alpha^2 \Gamma(1+2/\beta) \end{aligned}$$

$$\begin{aligned} \text{Thus } E(T^2) - (E(T))^2 &= \alpha^2 \Gamma(1+2/\beta) - (\alpha \Gamma(1+1/\beta))^2 \\ &= \alpha^2 [\Gamma(1+2/\beta) - (\Gamma(1+1/\beta))^2] \end{aligned}$$

$$\therefore \sigma^2 = \alpha^2 [\Gamma(1+2/\beta) - (\Gamma(1+1/\beta))^2] \tag{3.3}$$

The failure rate function for the Weibull is as defined for the exponential distribution. Nevertheless, the failure rate function is an increasing function if the failure time is described by a Weibull distribution with shape parameter $\beta > 1$. For this case we have

$$h(t) = \beta/\alpha(t/\alpha)^{\beta-1}$$

$$t \geq 0$$

PARAMETER ESTIMATION

One method through which the parameters can be estimated is by use of percentile. This is the method used in this project. Dubey (1967) proposed percentile estimators for both the shape (α) and the scale (β) parameters of the distribution based on two sample percentiles.

For any given p , $0 < p < 1$, the 100th percent percentile of the Weibull population is defined as the value $t = tp$ such that

$$F(tp) = 1 - \exp^{-(tp/\alpha)^\beta} = p \quad 3.4$$

The 100 percent percentile of the sample is denoted by y_p . From 3.4,

$$\log(1 - p) = -(tp/\alpha)^\beta$$

and

$$\log(-\log(1-p)) = \beta(\log tp - \log \alpha) \quad 3.5$$

so that for any two real numbers p_1 and p_2 with $0 < p_1 < p_2 < 1$ we have

$$\log(-\log(1-p_1)) = \beta(\log tp_1 - \log \alpha)$$

$$\text{and } \log(-\log(1-p_2)) = \beta(\log tp_2 - \log \alpha)$$

$$\Rightarrow \beta = \frac{\log(-\log(1-p_1)) - \log(-\log(1-p_2))}{\log tp_1 - \log tp_2}$$

$$\therefore \beta^* = \frac{\log(-\log(1-p_1)) - \log(-\log(1-p_2))}{\log y_{p_1} - \log y_{p_2}}$$

where β^* is the percentile estimator of β based on two ordered sample observations from a Weibull population.

From expression (3.5) the percentile estimator for α can be obtained in the following three ways

$$1. \quad \alpha^* = \exp / \log y_1 - \frac{\log(-\log(1-p_1))}{\beta^*}$$

$$2. \quad \alpha^* = \exp / \log y_2 - \frac{\log(-\log(1-p_2))}{\beta^*}$$

$$3. \quad \alpha^* = \exp / \frac{1}{2} \sum_{i=1}^2 \log y_i - \frac{\log(-\log(1-p_i))}{\beta^*}$$

The above three are identical and can be written as Dubey (1967)

$$\alpha^* = \exp / w \log y_1 + (1 - w) \log y_2 /$$

Where $W = 1 - \frac{\log K_1}{K}$

$$K = \log(-\log(1-p_1)) - \log(-\log(1-p_2)) \text{ and}$$

$$K_1 = -\log(1-p_1).$$

ILLUSTRATION

We shall now give some examples to demonstrate step by step, the procedure for obtaining the numerical values for the shape and scale parameters discussed in the last section.

$$1. \quad p_1 = 40\% \quad p_2 = 60\%$$

$$t_1 = 7 \text{ years} \quad t_2 = 10 \text{ years}$$

$$\begin{aligned} \text{Now } \beta^* &= \frac{\log(-\log(1-p_1)) - \log(-\log(1-p_2))}{\log y_1 - \log y_2} \\ &= \frac{\log(-\log(1-0.4)) - \log(-\log(1-0.6))}{\log 7 - \log 10} \end{aligned}$$

$$= \frac{-0.6717269 - (-0.0874215)}{1.944459101 - 2.3025851}$$

$$= 1.6382016$$

$$\alpha^* = \exp / w \log y_1 + (1 - w) \log y_2 /$$

$$\text{but } w = 1 - \frac{\log K_1}{K} = 1 - \frac{-0.6717269}{-0.5843054}$$

$$= 1 - 1.1495205 = -0.1495205$$

$$\alpha^* = \exp / -0.1495205 \times 1.9459101 + 1.1495205 \times 2.302585 /$$

$$= \exp / 2.3559152 /$$

$$= 10.54778$$

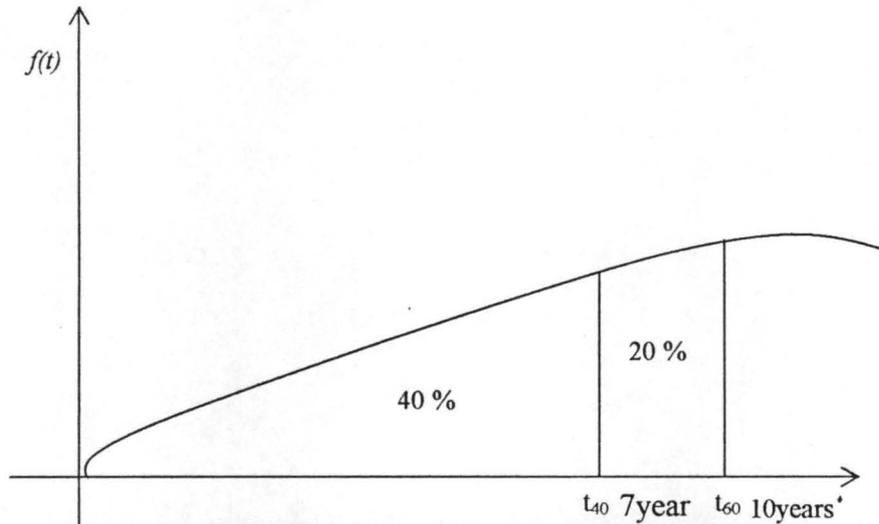


Figure 2: Graph for illustration 1 for the estimated values of α and β

$$2. \quad p_1 = 50\% \quad p_2 = 70\%$$

$$t_1 = 2 \text{ years} \quad t_2 = 3 \text{ years}$$

$$\beta = \frac{\log(-\log(0.5)) - \log(-\log(0.3))}{\log 2 - \log 3}$$

$$= 1.3617438$$

$$\alpha = \exp / 0.3361952 \times 0.6931471 + 0.6638047 \times 1.0986123 /$$

$$= \exp / 0.9622968 /$$

$$= 2.6177021$$

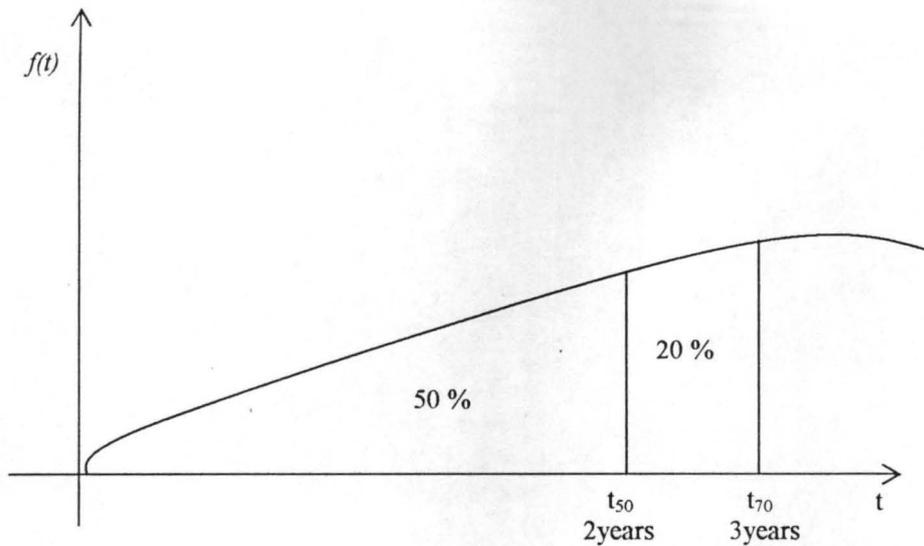


Figure 3: Graph for illustration for the estimated values of α and β

3. $p_1 = 60\%$ $p_2 = 80\%$
 $t_1 = 2 \text{ years}$ $t_2 = 4 \text{ years}$

$$\beta = \frac{\log(-\log(0.4)) - \log(-\log(0.2))}{\log 2 - \log 4}$$

$$= 0.8126794$$

$$\alpha = \exp / 0.8448065 \times 0.6931471 + 0.1551934 \times 1.3862944 /$$

$$= \exp / 0.8007191 /$$

$$= 2.2271419$$

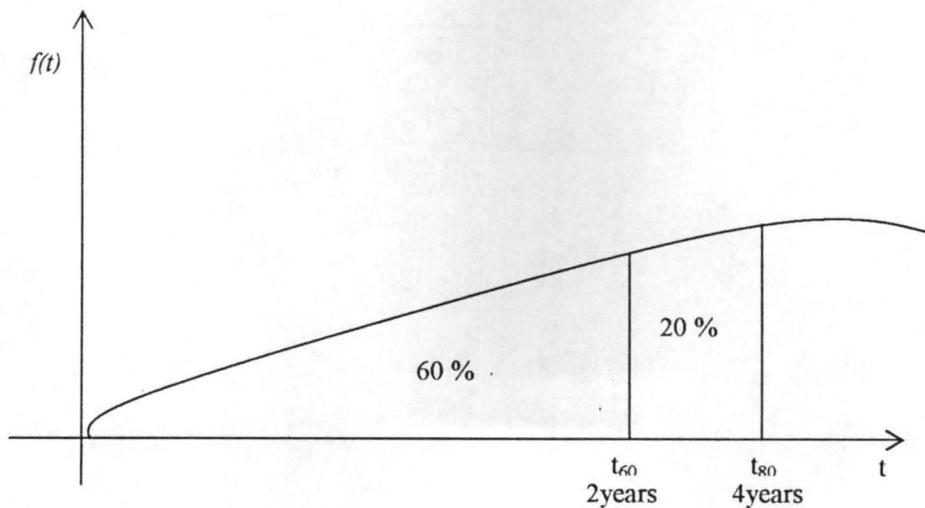


Figure 4: Graph for illustration 3 for the estimated values of α and β

The percentile points (p_1 and p_2) and the corresponding times (t_1 and t_2) for illustrations 1, 2, 3 and the estimated values for α and β are summarized in table 3.

Table 3: The percentile points and estimated values of the Weibull parameters

| Time | % of people | Time | % of people | Time | % of people |
|----------|-------------|----------|-------------|----------|-------------|
| 7 | 40 | 2 | 50 | 2 | 60 |
| 10 | 60 | 3 | 70 | 4 | 80 |
| α | 10.5 | α | 2.7 | α | 2.2 |
| β | 1.6 | β | 1.4 | β | 0.81 |

It must be noted that we have that $c = 0$. Thus the graphs lie on the origin as shown in figures 2, 3 and 4.

The Weibull distribution is prominent in applied sciences, mainly in the analysis of extreme value phenomena and in the field of reliability engineering. Karl (1975) The failure rate for the Weibull is not constant for $\beta \neq 1$. Therefore, it accurately measures the holding times in the states of a disease which changes with time.

The exponential and the Weibull distributions are prominent probability distributions. The relative advantage of the exponential distribution is that, it is specified by a single parameter and can be easily estimated from the mean. It also has the 'memoryless' property as explained in the previous section. The exponential distribution is a special case of the Weibull distribution when the shape parameter (β) is one. However, the failure rate function of the exponential distribution is constant, this does not accurately measure the holding times in the state of some diseases. For instance, the probability of an HIV positive individual to develop AIDS in 15 years (say) should be more than the probability of the individual developing AIDS in 3 years (say). According to the exponential distribution these probabilities are the same, hence the beauty of the Weibull distribution emerges. It defines an increasing function for the failure rate thereby taking care of the weakness of the exponential distribution.

3.13 MARKOV DECISION PROCESSES

Bhat in 1984 summarizes the definition of Markov decision processes thus; Markov decision processes bring together the study of sequential decision problems of statistics, and the dynamic programming technique of applied mathematics and operations research.

Consider a process that is observed at discrete time points to be in any one of m possible states, which we number by $1, 2, 3, \dots, m$. After observing the state of the process, an action must be chosen, and we let D , denote the set of all possible actions, we assume D is finite.

If the process is in state i at time n and action k is chosen, then the next state of the system is determined according to the transition probabilities ${}^k P_{ij}$.

Following Ross (1989), let X_n denote the state of the process at time n and K_n the action chosen at time n , then the above is equivalent to stating that

$$P(X_{n+1}=j | X_0, K_0, X_1, K_1, \dots, X_n=i, K_n=k) = {}^k P_{ij}$$

Thus the transition probabilities are dependent on the present state and subsequent action.

Definition (8): A policy; by a policy we mean a rule for choosing actions. A policy is a sequence of decisions, one for each state of the process.

Definition (9): Dynamic programming is an approach for optimizing multistage decision processes. It is based on Bellman's principle of optimality.

BELLMAN'S PRINCIPLE OF OPTIMALITY

An optimal policy has the property that regardless of the decisions taken to enter a particular state in a particular stage, the remaining decisions must constitute an optimal policy for leaving the state.

Consider a Markov chain with state space S . Suppose with every state we associate a decision to be chosen out of a set D .

Let ${}^k P_{ij}$ be the probability of the one step transition from i to j , $i, j \in S$ under decision $K \in D$.

Also we associate a reward ${}^k R_{ij}$ with decision K and transition i to j . Knowing the set of alternatives in the decision set and the corresponding

transition probabilities and rewards, the objective of the process is to select the optimal decision under certain criteria. When we associate rewards with every decision, maximization of expected reward over a given time horizon is the natural criterion.

If costs are associated with decisions; costs are essentially negative rewards and so minimization of expected costs is called for.

Let $V_i^{(n)}$ be the expected total earnings in n future transitions if decision K is made when the process is in state i . For the optimal decision $K=0$ if it exists; we have

$$V_i^{(n)} = \max_{k \in D} \sum_{j \in S} P_{ij}^k [R_{ij} + V_j^{(n-1)}], \quad n=1,2,3,\dots, i \in S \quad 3.5$$

This is a functional equation satisfied by the expected reward.

3.14 MARKOV REWARD PROCESSES

Consider an aperiodic, irreducible Markov chain with m states ($m < \infty$) and the transition probability matrix

$$P = \begin{bmatrix} P_{11} & P_{12} & \dots & P_{1m} \\ \cdot & \cdot & \cdot & \cdot \\ \cdot & \cdot & \cdot & \cdot \\ P_{m1} & P_{m2} & \dots & P_{mm} \end{bmatrix}$$

With every transition i to j associate a reward R_{ij} . If we let $V_i^{(n)}$ be the expected total earnings (reward) in the next n transitions, given that the system is in state i at present. A simple recurrence relation can be given for $\{V_i^{(n)}\}_{n=1}^{\infty}$ as follows:

$$V_i^{(n)} = \sum_{j=1}^m P_{ij} [R_{ij} + V_j^{(n-1)}], \quad i = 1,2,3,\dots,m, n = 1,2,\dots \quad 3.6$$

$$\text{Let } \sum_{j=1}^m P_{ij} R_{ij} = Q_i$$

Equation 3.6 can now be written as

$$V_i^{(n)} = Q_i + \sum_{j=1}^m P_{ij} V_j^{(n-1)} \quad 3.7$$

setting $n = 1, 2, \dots$. We get

$$V_i^{(1)} = Q_i + \sum_{j=1}^m P_{ij} V_j^{(0)}$$

$$\begin{aligned} V_i^{(2)} &= Q_i + \sum_{j=1}^m P_{ij} [Q_j + \sum_{k=1}^m P_{jk} V_k^{(0)}] \\ &= Q_i + \sum_{j=1}^m P_{ij} Q_j + \sum_{k=1}^m \sum_{j=1}^m P_{ij} P_{jk} V_k^{(0)} \\ &= Q_i + \sum_{j=1}^m P_{ij} Q_j + \sum_{k=1}^m P_{ik}^{(2)} V_k^{(0)} \end{aligned}$$

Where $P_{ij}^{(n)}$ is the (i,j) th element of the matrix P^n

$$\text{Let } V(n) = \begin{bmatrix} V_1^{(n)} \\ V_2^{(n)} \\ V_3^{(n)} \\ \vdots \\ V_m^{(n)} \end{bmatrix} \quad Q = \begin{bmatrix} Q_1 \\ Q_2 \\ Q_3 \\ \vdots \\ Q_m \end{bmatrix}$$

Equation (3.7) can be put in matrix notation as

$$V^{(2)} = Q + PQ + P^2 V^{(0)}$$

Extending this to a general n , we have

$$V^{(n)} = Q + PQ + P^2 Q + \dots + P^{(n-1)} Q + P^n V^{(0)}$$

$$= \left[I + \sum_{k=1}^{n-1} P^k \right] Q + P^n V^{(0)}$$

but $P_{ij}^{(n)} = \Pi_j + e_{ij}^{(n)}$

Where $\{\Pi_j\}_{j=1}^m$ is the limiting distribution of the Markov chain and

$$|e_{ij}^{(n)}| \leq cr^n$$

with $c > 0$ and $0 < r < 1$. therefore, as $n \rightarrow \infty$, $e_{ij}^{(n)} \rightarrow 0$ geometrically.

Let $\|e_{ij}^{(n)}\| = \eta(n)$

$$\text{And } \Pi = \begin{bmatrix} \Pi_1 & \Pi_2 & \Pi_m \\ \Pi_1 & \Pi_2 & \Pi_m \\ \cdot & \cdot & \cdot \\ \cdot & \cdot & \cdot \\ \Pi_1 & \Pi_2 & \Pi_m \end{bmatrix}$$

In Matrix notation, we can write P^n as

$$P^n = \Pi + \eta^{(n)}$$

Substituting this in (3.7) we get

$$\begin{aligned} V^{(n)} &= \left[I + \sum_{k=1}^{n-1} (\Pi + \eta^{(k)}) \right] Q + (\Pi + \eta^{(n)}) V^{(0)} \\ &= V^{(n)} + \left[\sum_{k=1}^{n-1} \eta^{(k)} \right] Q + n\Pi Q + \eta^{(n)} V^{(0)} \end{aligned} \tag{3.8}$$

In deriving (3.8), we have noted that $\eta^{(0)} = 1 - \Pi$

Now consider the sum

$$\sum_{k=0}^{n-1} \eta^{(k)} = \sum_{k=0}^{\infty} \eta^{(k)} - \sum_{k=n}^{\infty} \eta^{(k)} \tag{3.9}$$

It should be noted that each term in $\eta^{(k)}$ is less than or equal to cr^k ($c>0, 0<r<1$) in absolute value, and hence for large n the second term on the right hand side of (3.9) approaches an $m \times m$ matrix with zero elements. For the same reason the last term in (3.8) approaches a null matrix for large n .

Thus asymptotically we have

$$V_i^{(n)} = \prod V^{(0)} + \sum_{k=0}^{\infty} \eta^k Q + n \prod Q$$

which gives

$$V_i^{(n)} = \sum_{j=1}^m \prod_j V_j^{(0)} + \sum_{j=1}^m \gamma_{ij} Q_j + n \sum_{j=1}^m \Pi_j Q_j \quad 3.10$$

where we have written $\sum_{k=0}^{\infty} \eta^{(k)} = \|\gamma_{ij}\|$

writing

$$\sum_{j=1}^m \Pi_j V_j^{(0)} + \sum_{j=1}^m \gamma_{ij} Q_j = \beta_i$$

$$\sum_{j=1}^m \Pi_j Q_j = q$$

so that (3.10) can be put in the form

$$V_i(n) = \beta_i + nq$$

which shows that for large n , $V_i^{(n)}$ is a linear function of q for every i . Further, for different values of i , $V_i^{(n)}$ are represented by parallel straight lines with slope q and intercept β_i ($i = 1, 2, \dots, m$)

So far, we have considered the transition probability matrix P and the reward matrix R as given.

Instead, suppose that the decision maker has other alternatives and so is able to alter elements of P and R . To incorporate this feature, define D as the

decision set, and under decision $K \in D$ let KP_{ij} and KR_{ij} be the probability of the transition from i to j and the corresponding reward respectively for $KV_i^{(n)}$. The expected total earnings in n transitions under decision K ; we have the recurrence relations ($K=0$ represents the optimal decision)

$${}^0V_i^{(n)} = \max_{K \in D} \sum_{j=1}^m {}^kP_{ij} [{}^kR_{ij} + {}^0V_j^{(n-1)}] \quad n=1,2,\dots, i=1,2,\dots, m \quad 3.11$$

giving

$${}^0V_i^{(n)} = \max_{K \in D} \left[{}^kQ_i + \sum_{j=1}^m {}^kP_{ij} {}^0V_j^{(n-1)} \right] \quad i=1,2,\dots, m; n=1,2$$

where we have written $\sum_{j=1}^m {}^kP_{ij} {}^kR_{ij} = {}^kQ_i$

Recursive relation (3.11) gives an iteration procedure to determine the optimum decision $d_i^{(n)} \in D$. For $i=1,2,\dots, m$ and $n=1,2,\dots$

This is a Standard technique in Dynamic programming and it has been shown Bhat(1984) that this iteration process will converge on best alternative for each state as $n \rightarrow \infty$.

Since the procedure is based on the value of the policy (total earning) for any n , it is called the Value Iteration Method (VIM).

The method is based on recursively determining the optimum policy for every n , that would give the maximum value.

One major drawback of the method is that, there is no way to say when the policy converges into a stable policy; therefore, the value iteration procedure is useful only when n , is fairly small. This is the reason why it is appropriate for our diseases model as indicated in the following section.

CHAPTER FOUR

4.0 THE DEVELOPMENT OF THE MODELS

4.1 A THREE STATE MARKOV CHAIN MODEL FOR CATARRH DISEASE

A finite Markov chain is a discrete time parameter stochastic process in which the future state of the system is dependent only on the present state and is independent of the past history and the number of states are finite or countably infinite.

Suppose an individual has mild catarrh sometimes or severe catarrh some other time and most often has no symptoms of catarrh. We have the following three states if we should consider the disease catarrh as a Markov process.

State 1: No catarrh

State 2: Mild catarrh

State 3: Severe catarrh

It is assumed that the possibility of death due catarrh is very small and could be neglected. The classification of states for a Markov model is dependent on the nature of the process involved and the intended use of the model.

The transition diagram for this process is shown in the figure below

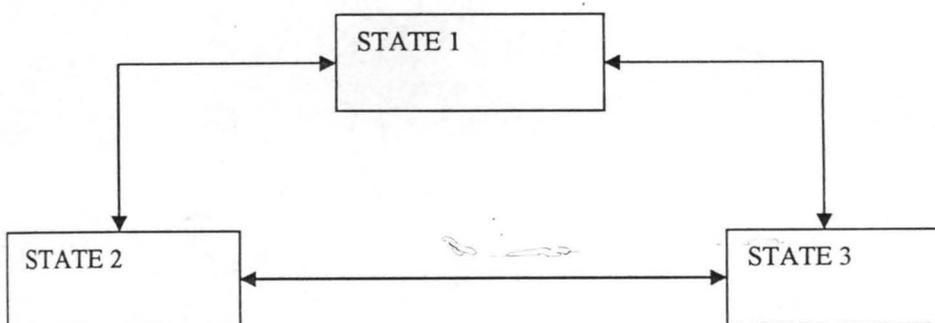


Figure 5: The state transition diagram for the process.

The transition between the states is described by the following transition probability matrix.

$$P = \begin{bmatrix} P_{11} & P_{12} & P_{13} \\ P_{21} & P_{22} & P_{23} \\ P_{31} & P_{32} & P_{33} \end{bmatrix}$$

Thus we define a Markov chain as a sequence X_0, X_1, \dots of random variables with the property that the conditional probability distribution of X_{n+1} given X_0, X_1, \dots, X_n depends only on the value of X_n but not further on X_0, X_1, \dots, X_{n-1} . that is, for any set of values h, i, \dots, j in discrete state space $P(X_{n+1} = j | X_0 = h, \dots, X_n = i) = P(X_{n+1} = j | X_n = i) = P_{ij}, j = 1, 2, 3$.

Let

$$P^n = (P_1^n, P_2^n, P_3^n)$$

denote the probabilities of finding the patient in any of the states 1, 2, 3 respectively on day n . then

$$P^n = P^{n-1}P \quad 4.1$$

on iteration, we have

$$P^n = P^0 P^n, n = 0, 1, 2, 3 \dots$$

where P^0 is any starting vector of probabilities.

The Markov chain analysis requires that the process be considered at discrete uniformly spaced intervals of time. It is assumed that the time between transitions is one day.

The fundamental assumption of Markov chain is that the probability of making a transition from state i to the j in the next time interval is a function of i and j and not of any history of the process before its arrival in state i .

4.2 THE LIMITING STATE PROBABILITIES

The state – occupation probabilities is independent of the starting state of the process if the number of time of the 'state transition' is large. Thus the process reaches a steady state after a sufficiently large period of time. This is the equilibrium probability distribution $\Pi = (\Pi_1, \Pi_2, \Pi_3)$ and letting $n \rightarrow \infty$ in equation (4.1)

we have

$$\Pi = \Pi P$$

and sum of the components of Π must be unity i.e.

$$\sum_{i=1}^3 \Pi_i = 1$$

we use these last two equations to find the limiting state probabilities for the process.

4.3 MODELLING THE EFFECT OF PREVENTIVE TREATMENT

A good measure of the effectiveness is obtained by defining

$$E_{ij} = (1 - k)P_{ij}, j = 2, 3$$

where k is a positive real number in the interval $[0, 1)$. Then

$$E_{11} = 1 - \sum E_{ij}, \quad 4.2$$

where $j = 2$ and 3 and the transition matrix is P with the first row replaced by E_{ij} , $j = 2$ and 3 .

4.4 MODELLING THE SEASONAL EFFECT

Suppose that the probable course and outcome of the catarrh disease changes with the seasons. We may consider two seasons as the transition times.

- (1) The wet season (April - October)
- (2) The dry season (November - March)

Each season has its own transition count and transition probability matrices.

We denote these as follows.

M_1 : Transition count matrix for Wet season

M_2 : Transition count matrix for Dry season

P_1 : Probability transition matrix for Wet season

P_2 : probability transition matrix for Wet season

Let

$$M_k = f_{ij}(k), \quad i, j = 1, 2, 3 \quad \text{and} \quad k = 1, 2.$$

$$\text{and } P_k = P_{ij}(k), \quad i, j = 1, 2, 3 \quad \text{and} \quad k = 1, 2.$$

$f_{ij}(k)$ denotes the transition count from state i to state j for the season

k . $P_{ij}(k)$ is the transition probability from state i to state j for the season

k .

Accordingly,

Accordingly,

$$\hat{P}_{ij}(k) = \frac{f_{ij}(k)}{f_i(k)}, \quad k = 1, 2 \text{ and } i, j = 1, 2, 3.$$

$$\text{where } f_i = \sum_{j=1}^3 f_{ij}(k) \quad 4.3$$

4.5 TEST FOR STATIONARITY OF THE PROBABILITY MATRICES P_K .

To test for independence of P_K on K , the Null hypothesis is stated thus

$$H_0: P_{ij}(k) = P_{ij}, \text{ for all } i, j = 1, 2, 3$$

$$H_1: P_{ij}(k) \text{ depends on } K.$$

The likelihood ratio Test for the above hypothesis, is

$$M = \sum_{k=1}^2 M_k = [f_{ij}] \quad 4.4$$

$$\text{where } f_{ij} = \sum_{k=1}^2 f_{ij}(k)$$

The maximum likelihood estimate of the stationary transition probability matrix

is

$$P_{ij} = \frac{f_{ij}}{f_i} \quad 4.5$$

$$\text{where } f_i = \sum_{j=1}^3 f_{ij}$$

The λ , the likelihood ratio criterion is given by

$$\lambda = \prod_{i,j=1}^3 \prod_{k=1}^2 \left[\frac{P_{ij}}{P_{ij}(k)} \right]^{f_{ij}(k)}$$

According to Bhat (1984)

$$-2 \ln \lambda = \chi_{m(m-1)(T-1)}^2$$

where m is the number of states and T is the time parameter. We evaluate λ , and calculate $-2 \ln \lambda$. We then get the critical value of χ^2 at α significance level and compare it with $-2 \ln \lambda$. It is then decided to accept or reject the Null hypothesis. With the acceptance of H_0 , we have a homogeneous Markov chain model. The model is represented by a single transition count matrix in (4.4) and the P_{ij} s are estimated from (4.5). Otherwise we have the non-homogeneous Markov chain model.

4.6 NON – HOMOGENEOUS MARKOV CHAIN MODEL

Following Howard (1971), the stochastic matrix P can be written as $P = P_1 P_2$ and the P_{ij} s are estimated from (4.3).

The limiting state probability vector Π_1 and Π_2 for the two seasons are then obtained from the following

$$\begin{aligned}\Pi_1 &= \Pi_0 P_1 \\ \Pi_2 &= \Pi_1 P_2\end{aligned}$$

it is observed that $\Pi_0 = \Pi_2$

4.7 DISCRETE STATE AND CONTINUOUS TIME MARKOV MODELLING FOR CATARRH DISEASE.

In the previous section we considered the catarrh disease as a Markov process in discrete state and time. We shall now consider the three state model of the disease in continuous time, which will enable us to obtain information about the patient at any given point in time.

Following the work of Howard in 1960, we let a_{ij} represent the transition rate of the patient from state i to state j , $i \neq j$. In a short time interval

($t, t + \Delta t$), the patient currently in state i will make a transition to state j with probability $a_{ij} \Delta t, i \neq j$. if X_t is the state of the process at time t , then we have

$$P(X_{t+\Delta} = j | X_t = i) = a_{ij} \Delta t.$$

The probability of two or more state transitions is of order $(\Delta t)^2$ or more and it is negligible if Δt is sufficiently small.

Suppose that the transition rates do not change with time (a_{ij} 's are constants).

and

$$a_{jj} = - \sum_{i \neq j} a_{ji}, \quad i, j = 1, 2, 3 \quad 4.6$$

We describe the process by a transition – rate matrix A with components a_{ij} .

Suppose $P_i(t)$ is the probability that the patient is in the state i at time t after the start of the process and let $P_j(t + \Delta t)$ be the probability that the patient will be in state j a short time Δt later.

Then,

$$P_j(t + \Delta t) = P_j(t) \left(1 - \sum_{i \neq j} a_{ij} \Delta t \right) + \sum_{i \neq j} P_i(t) a_{ij} \Delta t \quad j = 1, 2, 3 \quad 4.7$$

Equation (4.7) can be explained thus: There are basically two mutually exclusive ways in which the patient can be in state j at time $(t + \Delta t)$ first, he could have been in state j at the time t and make no transition during the interval. ($t, t + \Delta t$) These events have probabilities $P_j(t)$ and $1 - \sum_{i \neq j} a_{ij} \Delta t$ since the probability of multiple transition is of the order higher than Δt and is

negligible. The probability of making no transition in $(t, t + \Delta t)$ is 1, minus the probability of making a transition in $(t, t + \Delta t)$ to some $i \neq j$

Another way that the patient could be in state j at time $t + \Delta t$ is to have been in state $i \neq j$ at time t and then make a transition from i to j during the time Δt .

Equation (4.7) is obtained by multiplying the probabilities and adding over all i that are not equal to j because the patient could have entered j from any other state i putting (4.6) in (4.7) and rearranging terms gives

$$P_j(t + \Delta t) - P_j(t) = \sum_{i=1}^3 P_i(t) a_{ij} \Delta t$$

Thus we have

$$\frac{dP_j(t)}{dt} = \sum_{i=1}^3 P_i(t) a_{ij} \quad j = 1, 2, 3$$

in matrix form, we have

$$\frac{d}{dt} P(t) = P(t)A. \quad 4.8$$

$P(t)$ is a row vector of state probabilities at time t .

To obtain the solution to (4.8), the initial condition

$$P_i(0), \quad i = 1, 2, 3; \text{ must be specified.}$$

Taking the Laplace transform of (4.8) we have

$$P(s) = P(0)(SI - A)^{-1}$$

Thus $P(t)$ is obtained as the inverse transform of $P(s)$.

In fact, equation (4.8) is an exact (not approximate) differential equations for

$P_{ij}(t)$ in $\frac{dP_{ij}(t)}{dt} = \sum p_{ik(t)} a_{kj}$ (Chapman Kolmogorov equation). It is a linear, first-

order differential equation with constant coefficients – the a_{jk} 's. in this particular

case, they are simple enough to solve directly. Making use of whatever

manipulations or solution technique we find most convenient (apart from the

one proposed above) and using the initial conditions $P_{ij}(0) = 0$ for $i \neq j$ and

$P_{ij}(0) = 1$ for $i = j$

4.8 MODELLING THE EFFECT OF PREVENTIVE TREATMENT

Following Korve(2000), suppose the catarrh patient is in state 1 at time

t , then he has probabilities of $a_{12} \Delta t$ and $a_{13} \Delta t$ of making a transition to

state 2 and state 3 respectively. This means that the times taken for the patient

to make a transition from state 1 to states 2 and 3 are exponentially distributed

with mean $\frac{1}{a_{12}}$ and $\frac{1}{a_{13}}$ respectively.

When preventive treatment is given these mean times are increased to $\frac{1}{b_{12}}$

and $\frac{1}{b_{13}}$, respectively. And the probabilities of making transition from state 1

and 3 in $(t, t + \Delta t)$ are reduced by $b_{12} \Delta t$ and $b_{13} \Delta t$ respectively.

The measure of this effectiveness is obtained from the following expression

$$\frac{1}{b_{1j}} = (1 + k) \frac{1}{a_{1j}}, \quad j = 2, 3$$

where k is a positive real number. If $k = 0$, the treatment has no effect and if $k >$

0 the treatment has effect.

We let

$$b_{21} = a_{21} \quad \text{and} \quad b_{31} = a_{31}$$

and the b_{ij} 's are obtained from (4.6) and in (4.8) we have

$$\frac{d}{dt} P(t) = P(t)B. \quad 4.9$$

The matrix B has components b_{ij} , $i, j = 1, 2, 3$.

4.9 A SEMI-MARKOV MODEL FOR LEPROSY DISEASE

In this chapter we considered leprosy as a disease where the transition of people from one state of the disease to another may not necessarily occur at discrete time instants. We therefore look at a situation where the time between transitions may be in several units of time interval, and where the transition time can depend on the transition being made. This leads us to a generalization of a Markov process called the semi-Markov process (Howard, 1971). In other words we shall consider the disease leprosy as a semi-Markov process running in discrete time and continuous time respectively.

One other mathematical definition of a Markov chain is a sequence X_0, X_1, \dots of discrete random variables with the property that the conditional probability distribution of X_{n+1} given X_0, X_1, \dots, X_n depend only on the value of X_n but not further on X_0, X_1, \dots, X_{n-1} . That is for any set of values, h, i, \dots, j in the discrete state space,

$$P(X_{n+1} = j | X_0 = h, \dots, X_n = i) = P(X_{n+1} = j | X_n = i) = P_{ij}, \quad i, j = 1, 2, 3, 4$$

The matrix P whose entries are the P_{ij} 's is called the transition probability matrix for the process. The above chain is a first order Markov chain. In this process, the probability of making transition to a future state does not depend

on the previous states but only depends on the present state. In other words, the probability of making a transition to a future state does not depend on the past history.

The matrix P and the initial state transition probabilities completely specify the process. If the transition probabilities depend on time, then the Markov chain is non-homogeneous, otherwise, it is homogeneous. In this project we shall only consider the Markov chain that does not depend on time. Thus we have stationary transition probabilities.

The Markov process discussed above has the property that state changes can only occur at the appropriate time instants. However, given the nature of the disease leprosy, transition may not actually occur at these time instants. We therefore consider a 'situation' where the time between transition may be several of units of time and where the transition time can depend on the transition that is being made. This leads to a general form of Markov process called a semi-Markov process (Howard, 1971). In section 4.2 we use the characteristics of a semi-Markov process to develop a model for the control of leprosy.

4.10 THE DEVELOPMENT OF THE MODEL

In this section we shall develop a semi-Markov model for leprosy. The assumptions of the model are made in section 4.11, the model is formulated in section 4.12. Interval transition probabilities are given in section 4.13 and effectiveness of treatment is considered in section 4.14.

4.11 MODEL ASSUMPTIONS

Leprosy is considered as a disease that runs in time. Some suitable states of the disease are specified and the description of the manner in which the patient moves from one state to another is given. The states of the disease are finite. It should be readily observed that there is no unique set of states and the progress of the people through the states can be described in a variety of ways. The choice of states should therefore be governed by the intended use of the model and the availability of data.

The basic assumption in developing the model is that the transition from one state to a different state should not occur at time $t = 0$ (year 0) and that the basic unit of time is one year.

A leprosy patient that dies during treatment is assumed to die of leprosy. Natural death is not considered.

A patient that fails to recover from treatment after completing a session of treatment has developed a resistance to the drug and is consequently considered to develop a relapse from the state of treatment.

4.12 FORMULATION OF THE MODEL

We consider a leprosy patient. Let us assume that each year the leprosy patient is under treatment or has recovered from the disease or has relapsed or has died from the disease. We therefore have a four state process.

State 1 - Under treatment

State 2 - Recovery

State 3 - Relapse

State 4 - Death due to leprosy.

These states are assumed to be mutually exclusive and exhaustive. The transition from one state to another is indicated in the transition diagram shown in figure 6.

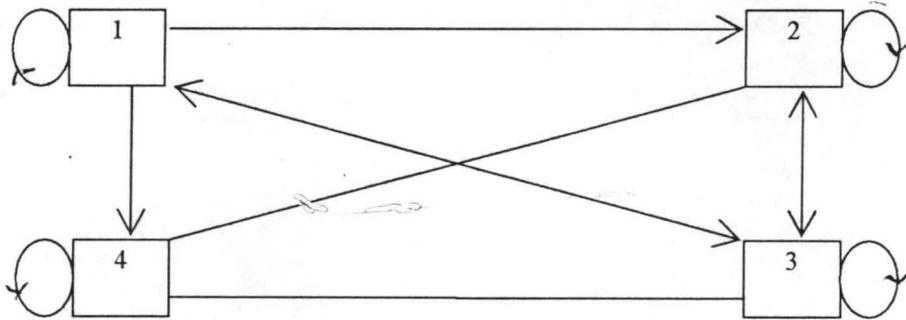


Figure 6: Transition diagram for leprosy.

We observe that states 1, 2 and 3 are transient states and state 4 is an absorbing state. In other words, all possible transitions of the process are made between states 1, 2 and 3 but once a transition is made to state 4 the process terminates. We would like a transition to occur at a time the duration of stay in a state is completed, even if the new state is the same as the old. Such a transition is called virtual transition, and are represented by loops in the transition diagram.

From the above transition diagram we can record the transition probability matrix ' P ' for the process as shown below.

$$P = \begin{bmatrix} P_{11} & P_{12} & P_{13} & P_{14} \\ 0 & P_{22} & P_{23} & 0 \\ P_{31} & P_{32} & P_{33} & 0 \\ 0 & 0 & 0 & P_{44} \end{bmatrix}$$

We use the semi-Markov process technique to analyse the process with the above set of states. The transitions can be readily identified from the transition diagram shown in figure 5 or from the transition probability matrix P .

To study this process, we have to specify the probabilistic nature of the transition. We shall think of this process as a process whose successive state occupancies are governed by the transition probabilities of a Markov chains, but whose stay in any state is described by a random variable that depends on the state to which the next transition is made.

In precise terms, let P_{ij} be the probability that the leprosy patient who is in state ' i ' on his last transition will enter state ' j ' on his next transition, $i, j = 1, 2, 3, 4$. The transition probabilities must satisfy the following

$$P_{ij} \geq 0, i, j = 1, 2, 3, 4.$$

$$\text{and } \sum_{j=1}^4 P_{ij} = 1, \quad i = 1, 2, 3, 4.$$

whenever the patient enters state ' i ' he remains there for a time T_{ij} in state i before making a transition to state ' j '. T_{ij} is called the 'holding time' in state i . The holding times are positive integer valued random variables each governed by a probability distribution function $f_{ij} ()$ called the holding time distribution function for a transition from state i to state j .

$$\text{Thus } P(T_{ij} = m) = f_{ij}(m). \quad m = 1, 2, 3, \dots$$

$$i, j = 1, 2, 3, 4.$$

We assume that the means μ_{ij} of all holding time distribution are finite and that all holding times are at least one year in length. That is,

$$f_{ij}(0) = 0$$

To completely describe the semi-Markov process we must specify four holding time distribution functions in addition to the transition probabilities. For a fixed value of i T_{ij} is the same for each value of j , ($i, j = 1, 2, 3, 4$).

Figure 7 shows a portion of a possible trajectory for the leprosy patient.

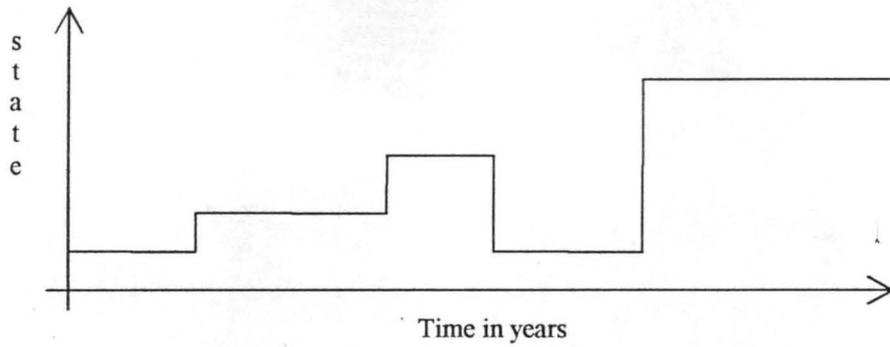


Figure 7. A possible trajectory for the process

Let $F_{ij}(\cdot)$ be the probability distribution of T_{ij} .

$$F_{ij}(n) = P(T_{ij} \leq n) = \sum_{m=\phi}^n f_{ij}(m)$$

and $\bar{F}_{ij}(\cdot)$ be the complementary probability distribution of T_{ij} .

$$\bar{F}_{ij}(n) = 1 - F_{ij}(n) = P(T_{ij} > n) = \sum_{m=n+1}^{\infty} f_{ij}(m)$$

Suppose the patient enters state i . Let Y_i be the time he spent in state i before moving out of the state i . Then Y_i is called the waiting time in state i .

We let $w_i(\cdot)$ be the probability distribution function of Y_i . Then

$$w_i(m) = P(Y_i = m) = \sum_{j=1}^4 P_{ij} f_{ij}(m)$$

The probability distribution $W_i(\cdot)$ and the complementary cumulative probability distribution $\bar{W}_i(\cdot)$ for the waiting times are given as follows

$$\begin{aligned} W_i(m) &= P(Y_i \leq n) = \sum_{m=1}^n W_i(m) \\ &= \sum_{m=1}^n \sum_{j=1}^4 P_{ij} f_{ij}(m) \\ &= \sum_{j=1}^4 P_{ij} F_{ij}(n) \end{aligned}$$

and

$$\bar{W}_i(n) = P(Y_i > n) = 1 - W_i(n) = \sum_{m=n+1}^{\infty} w_i(m)$$

$$\begin{aligned}
&= \sum_{m=n+1}^{\infty} \sum_{j=1}^4 P_{ij} f_{ij}(m) \\
&= \sum_{j=1}^4 P_{ij} \bar{F}_{ij}(n) \quad 4.9
\end{aligned}$$

4.13 INTERVAL TRANSITION PROBABILITIES

We define $\phi_{ij}(n)$ to be the probability that the patient will be in state j in year n given that he entered state i in year zero. This is called the interval transition probability from state i to state j in the interval $(0, n]$. Then

$$\phi_{ij}(n) = \delta_{ij} \bar{W}_i(n) + \sum_{k=1}^4 P_{ik} \sum_{m=1}^n f_{ik}(m) \phi_{kj}(n-m)$$

$$\delta_{ij} = \begin{cases} 1 & i=j \\ 0 & i \neq j \end{cases}$$

$$i, j = 1, 2, 3, 4, \quad n = 1, 2, 3, \dots$$

$\bar{W}_i(n)$ is as defined in (4.9).

4.14 EFFECTIVENESS OF TREATMENT

When the leprosy patient undergoes treatment, it is expected that this treatment should have an effect on the disease. This effect should be noticed in the increase in probability of recovery, a decrease in the probabilities of death and having a relapse. An appropriate measure of this treatment effectiveness is obtained from the following expressions.

$$E_{12} = (1 + k)P_{12}$$

$$E_{1j} = (1 - k)P_{1j}, \quad j = 3, 4$$

when k is a positive real number in the interval $[0, 1)$. Then

$$E_{11} = 1 - \sum_{j=2}^4 E_{1j}$$

and the transition matrix is P with the first row replaced by E_{1j} . $J = 1, 2, 3, 4$.

4.15 SEMI - MARKOV MODEL IN CONTINUOUS TIME

In the last section we have considered the disease leprosy in discrete states and time. We should think of the same process in discrete state but in continuous time.

The continuous time case has essentially the same properties as the discrete time in respect to the transition probabilities of the Markov chains, the holding times and their probability distribution functions.

Let $f_{ij}(\cdot)$ be the probability distribution of continuous random variable T_{ij}

$$F_{ij}(n) = P(T_{ij} \leq n) = \int_{m=0}^n f_{ij}(m) dm$$

And $\bar{F}_{ij}(\cdot)$ be the complementary cumulative probability distribution of T_{ij} ,

$$\bar{F}_{ij}(\cdot) = 1 - f_{ij}(n) = P(T_{ij} > n) = \int_{m=n+1}^{\infty} f_{ij}(m) dm$$

Suppose the patient enters state i . Let Y_i be the time he spent in state i before moving out of the state i . Then Y_i is called the waiting time in state i .

we let $w_i(\cdot)$ be the probability distribution function of Y_i .

$$\text{Then } w_i(m) = P(Y_i = m) = \sum_{j=1}^4 P_{ij} f_{ij}(m)$$

The probability distribution $w_i(\cdot)$ and the complementary probability distribution $\bar{w}_i(\cdot)$ for the waiting times are given as follows

$$w_i(n) = P(Y_i \leq n) = \int_{m=1}^n w_i(m) dm$$

$$= \sum_{j=1}^4 P_{ij} F_{ij}(n)$$

$$\text{and } \bar{w}_i(n) = P(Y_i > n) = 1 - w_i(n)$$

$$= \int_{m=n+1}^{\infty} w(m) dm$$

$$= \sum_{j=1}^4 P_{ij} \bar{F}_{ij}(n)$$

4.16 INTERVAL TRANSITION PROBABILITY

The interval transition probability is defined thus:

$$\phi_{ij}(n) = \delta_{ij} \bar{w}_i(n) + \sum_{k=1}^4 P_{ik} \int_1^n f_{ik}(m) \phi_{kj}(n-m) dm$$

$$\delta_{ij} = \begin{cases} 1 & i=j \\ 0 & i \neq j \end{cases} \quad i, j = 1, 2, 3, 4, n = 1, 2, 3, \dots$$

This is the interval transition probability from state i to state j in the interval $(0, n]$.

4.17 OPTIMAL MARKOV MULTIDRUG DECISION PROCESSES FOR THE CONTROL OF CATARRH AND LEPROSY DISEASES

FORMULATION OF THE DECISION MODEL

So far, we have not taken into account the possible cost of control (treatment) of the diseases (catarrh and leprosy) considered in this project. However, we shall introduce the concept of Markov decision process as it may affect the patients or the medical personnel's in the choice of drug for administration.

At any given point in time and state of the process. The patient has an opportunity or a privilege to make a choice of the possible combination of drugs.

The choice of drugs may however be dependent on:

- (1) Availability of the drugs
- (2) Resources available to the patient
- (3) The state or severity of the disease.

For the sake of simplicity let us divide the drugs into two groups as follows:

- (1) Low priced drugs
- (2) high priced drugs

From every day experience, it is known that low priced drugs are less costly and are often administrated for longer duration of time. Whereas, the high priced drugs are usually more costly and are often administered for a shorter period of time.

Suppose that the following alternatives exist for the three states:

State 1:

Alternative 1: Self medication/self care

Alternative 2: Go to see a doctor

State 2:

Alternative 1: Low priced drugs

Alternative 2: high priced drugs

State 3:

Alternative 1: Continue without change of drugs

Alternative 2: Change drugs

Costs are usually associated with each of these alternatives.

Our objective is to obtain the policy or alternative that minimizes the costs of the control of the diseases at any given state and time in the control process of the diseases.

Thus instead of considering the cost of individual drug to be administered, we shall consider the cost of a combination of drugs to be administered at any given state and time of the diseases.

4.18 ASSUMPTIONS

Markov reward process requires that the Markov chain to be a periodic irreducible and positive recurrent. (ergodicity). We thus assumed that the three-state Markov chain for catarrh diseases is ergodic.

For the four-state model for the leprosy disease, records have shown that death due to leprosy is uncommon, although not impossible. The usual terminal event is the deformity of fingers, toes etc or tuberculosis.

On the basis of that, we assume that death due to leprosy is rare and could be neglected. Thus we have a three state model for leprosy.

4.19 MODEL IMPLEMENTATION

Let the transition probabilities (P_{ij}) and the corresponding reward (R_{ij}) be given as follows:

$$P = (P_{ij}) = \begin{bmatrix} P_{11} & P_{12} & P_{13} \\ P_{21} & P_{22} & P_{23} \\ P_{31} & P_{32} & P_{33} \end{bmatrix} \quad i, j = 1, 2, 3$$

and

$$R = (R_{ij}) = \begin{bmatrix} R_{11} & R_{12} & R_{13} \\ R_{21} & R_{22} & R_{23} \\ R_{31} & R_{32} & R_{33} \end{bmatrix} \quad i, j = 1, 2, 3$$

Let D be the decision set as defined in the previous section so that in every state of the diseases we have two alternative decisions available to the patient.

That is, Alternative 1; and Alternative 2; Thus in every state we have $k=1, 2 \in D$.

We shall now determine the best policies for every n using

$$\begin{aligned} {}^0V_i^{(n)} &= \min_{k \in D} \sum_{j=1}^m {}^k P_{ij} \left[{}^k R_{ij} + {}^0V_j^{(n-1)} \right] \\ &= \min_{k \in D} \left[{}^k Q_i + \sum_{j=1}^m {}^k P_{ij} {}^0V_j^{(n-1)} \right] \end{aligned}$$

Let ${}^0V_i^{(0)} = 0$ for $i=1, 2, 3$. Then for $n=1$, we have

$${}^1Q_1 = {}^1P_{11} {}^1R_{11} + {}^1P_{12} {}^1R_{12} + {}^1P_{13} {}^1R_{13} = \alpha_1$$

$${}^1Q_2 = {}^1P_{21} {}^1R_{21} + {}^1P_{22} {}^1R_{22} + {}^1P_{23} {}^1R_{23} = \alpha_2$$

$${}^1Q_3 = {}^1P_{31} {}^1R_{31} + {}^1P_{32} {}^1R_{32} + {}^1P_{33} {}^1R_{33} = \alpha_3$$

We shall now implement the second alternative for the three states. Thus, we get

$${}^2Q_1 = {}^2P_{11} {}^2R_{11} + {}^2P_{12} {}^2R_{12} + {}^2P_{13} {}^2R_{13} = \alpha_4$$

$${}^2Q_1 = {}^2P_{21} {}^2R_{21} + {}^2P_{22} {}^2R_{22} + {}^2P_{23} {}^2R_{23} = \alpha_5$$

$${}^2Q_1 = {}^2P_{31} {}^2R_{31} + {}^2P_{32} {}^2R_{32} + {}^2P_{33} {}^2R_{33} = \alpha_6$$

The value of $\alpha_i, i = 1, 2, 3, 4, 5, 6$ will determine which of the alternatives minimizes our cost for $n=1$. Since we are concerned about minimizing the costs of drugs to be administered; the alternative that yields least value of $\alpha_i, i = 1, 2, 3, 4, 5, 6$ constitutes the best policy for $n=1$, that is, if the least value occurs between $\alpha_i, i = 1, 2, 3$. then alternative 1 constitutes the best policy thus

$${}^0V_i^{(1)} = \min_{1,2} {}^kQ_i \text{ and hence}$$

$$d_1^{(1)} = 1 \text{ and } d_2^{(1)} = 1$$

Now let ${}^0V_1^{(1)}$ and ${}^0V_2^{(1)}$ be the minimum cost/reward corresponding to $d_1^{(1)}$ and $d_2^{(1)}$ respectively.

For $n = 2$ we have

$${}^0V_i^{(2)} = \min_{1,2} [{}^kQ_i + \sum {}^kP_{ij} {}^0V_j^{(1)}] \quad i,j$$

And the iteration continues for $n = 3, 4, 5, \dots$

The successful use of these models developed here would require joint work by the medical personnel and applied mathematician. The problem of communication between these two groups of people is greatly reduced by not using advanced mathematics.

CHAPTER FIVE

5.0 APPLICATION OF THE MODELS, RESULTS AND DISCUSSIONS

5.1 APPLICATION OF MARKOV CHAIN MODELS.

The following transition counts were recorded for forty-seven individuals during the wet season and dry season respectively. Since the Markov chain requires the process to change at a given unit of time interval. Our unit of time is one day.

TABLE 4. Transition count for wet season

| | | ACTUAL DAY | | | |
|---------------|---------|------------|---------|---------|----|
| | | STATE 1 | STATE 2 | STATE 3 | |
| PRECEDING DAY | STATE 1 | 19 | 1 | 2 | 22 |
| | STATE 2 | 2 | 9 | 4 | 15 |
| | STATE 3 | 1 | 2 | 7 | 10 |
| | TOTAL | | | | 47 |

TABLE 5. Transition count for dry season

| | | ACTUAL DAY | | | |
|---------------|---------|------------|---------|---------|----|
| | | STATE 1 | STATE 2 | STATE 3 | |
| PRECEDING DAY | STATE 1 | 12 | 2 | 3 | 17 |
| | STATE 2 | 6 | 6 | 7 | 19 |
| | STATE 3 | 1 | 2 | 8 | 11 |
| | TOTAL | | | | 47 |

We obtain the transition count matrix for the two seasons

Thus $(42106)^2 (0.095238095 / 0.1)^2 (0.19047619 / 0.2)^2 (0.114285714 / 0.7)^2$

$$M_1 = \begin{bmatrix} 19 & 1 & 2 \\ 2 & 9 & 4 \\ 1 & 2 & 7 \end{bmatrix}, \quad P_1 = \begin{bmatrix} 0.864 & 0.045 & 0.091 \\ 0.133 & 0.600 & 0.267 \\ 0.100 & 0.200 & 0.700 \end{bmatrix}$$

$$M_2 = \begin{bmatrix} 12 & 2 & 3 \\ 6 & 6 & 7 \\ 1 & 2 & 8 \end{bmatrix}, \quad P_2 = \begin{bmatrix} 0.706 & 0.118 & 0.176 \\ 0.316 & 0.316 & 0.368 \\ 0.091 & 0.182 & 0.727 \end{bmatrix}$$

Therefore

the critical value of χ^2 at $\alpha = 0.05$ is 12.59

$$M = \begin{bmatrix} 31 & 3 & 5 \\ 8 & 15 & 11 \\ 2 & 4 & 15 \end{bmatrix}, \quad P = \begin{bmatrix} 0.795 & 0.077 & 0.128 \\ 0.235 & 0.441 & 0.324 \\ 0.095 & 0.190 & 0.714 \end{bmatrix}$$

$$\lambda = \prod_{i,j=1}^3 \prod_{k=1}^2 \left[\frac{P_{ij}^{(k)}}{P_{ij}^{(1)}} \right]^{f_{ij}^{(k)}}$$

$$= (P_{11}/P_{11}^{(1)})^{f_{11}^{(1)}} (P_{12}/P_{12}^{(1)})^{f_{12}^{(1)}} (P_{13}/P_{13}^{(1)})^{f_{13}^{(1)}} (P_{11}/P_{11}^{(2)})^{f_{11}^{(2)}} (P_{12}/P_{12}^{(2)})^{f_{12}^{(2)}} (P_{13}/P_{13}^{(2)})^{f_{13}^{(2)}}$$

$$(P_{21}/P_{21}^{(1)})^{f_{21}^{(1)}} (P_{22}/P_{22}^{(1)})^{f_{22}^{(1)}} (P_{23}/P_{23}^{(1)})^{f_{23}^{(1)}} (P_{21}/P_{21}^{(2)})^{f_{21}^{(2)}} (P_{22}/P_{22}^{(2)})^{f_{22}^{(2)}} (P_{23}/P_{23}^{(2)})^{f_{23}^{(2)}}$$

$$(P_{31}/P_{31}^{(1)})^{f_{31}^{(1)}} (P_{32}/P_{32}^{(1)})^{f_{32}^{(1)}} (P_{33}/P_{33}^{(1)})^{f_{33}^{(1)}} (P_{31}/P_{31}^{(2)})^{f_{31}^{(2)}} (P_{32}/P_{32}^{(2)})^{f_{32}^{(2)}} (P_{33}/P_{33}^{(2)})^{f_{33}^{(2)}}$$

$$= (0.7987181 / 0.863636)^{19} (0.7692308 / 0.4545455)^1 (0.12820513 /$$

$$0.090909090909)^2 (0.79487178 / 0.70588235)^{12} (0.7692308 / 0.11767706)^2$$

$$(0.12820513 / 0.17647059)^3 (0.2352412 / 0.133333)^2 (0.44117647 / 0.6)^9$$

$$(0.32352941 \times 0.2666667)^7 (0.4411764 \times 0.31578949)^4 (0.32352941 \times 0.36842106)^7 (0.095238095 \times 0.1)^1 (0.19047619 \times 0.2)^2 (0.714285714 \times 0.7)^7 (0.095238095 \times 0.9090909)^1 (0.19047619 \times 0.18181818)^2 (0.714285714 \times 0.72727273)^8$$

$$\lambda = 0.10205577$$

Here $m = 3$, $T = 2$

Therefore

$$-2 \ln \lambda = \chi^2_{3(3-1)} = \chi^2_6$$

$$-2 \ln \lambda = 4.564867465 = \chi^2_6$$

the critical value of χ^2_6 at $\alpha = 0.05$ is 12.59

Therefore the null hypothesis of constant transition probability matrix cannot be rejected.

The test statistic as shown above indicates that the two seasons from which the data were obtained are stationary. That is to say that the occurrence of catarrh disease in the two seasons is fairly uniform.

It is therefore very important to mention at this point that catarrh disease is Not Seasonal. We shall now proceed to obtain the result for the model using this preliminary result.

The model can be represented by a single transition count matrix. Thus the maximum likelihood estimate of the transition probability matrix is given thus:

$$P = \begin{pmatrix} 0.795 & 0.077 & 0.128 \\ 0.235 & 0.441 & 0.324 \\ 0.095 & 0.190 & 0.714 \end{pmatrix} \text{ corrected to 3 dp}$$

calculating P^n , we have

$$P^3 = \begin{pmatrix} 0.575 & 0.145 & 0.280 \\ 0.359 & 0.223 & 0.419 \\ 0.259 & 0.226 & 0.515 \end{pmatrix}$$

$$P^6 = \begin{pmatrix} 0.455 & 0.179 & 0.366 \\ 0.395 & 0.196 & 0.409 \\ 0.363 & 0.204 & 0.432 \end{pmatrix}$$

$$P^{10} = \begin{pmatrix} 0.416 & 0.190 & 0.394 \\ 0.405 & 0.193 & 0.402 \\ 0.399 & 0.195 & 0.407 \end{pmatrix}$$

$$P^{13} = \begin{pmatrix} 0.409 & 0.192 & 0.399 \\ 0.406 & 0.193 & 0.401 \\ 0.404 & 0.193 & 0.401 \end{pmatrix}$$

$$P^{16} = \begin{pmatrix} 0.408 & 0.192 & 0.400 \\ 0.407 & 0.193 & 0.401 \\ 0.406 & 0.193 & 0.401 \end{pmatrix}$$

$$= \begin{pmatrix} 0.41 & 0.19 & 0.40 \\ 0.41 & 0.19 & 0.40 \\ 0.41 & 0.19 & 0.40 \end{pmatrix} \text{ corrected to 2dp} \quad 5.1$$

and for $n > 16$, we find that P^n gets closer and closer to exactly (5.1) that is, as n increases.

$$P^n = P^0 P^n$$

$$= (P^0_1 P^0_2 P^0_3) \begin{pmatrix} 0.41 & 0.19 & 0.40 \\ 0.41 & 0.19 & 0.40 \\ 0.41 & 0.19 & 0.40 \end{pmatrix}$$

$$= (0.41 \ 0.19 \ 0.40)$$

Again as n increase this approximation becomes more and more accurate.

That is

$$P^n \rightarrow (0.41 \ 0.19 \ 0.40)$$

The limit state probability vector is given by

$$\pi = \pi p = (0.41 \ 0.19 \ 0.40)$$

This shows that in the long run 41% of the individual will have no catarrh. 19% will have mild catarrh and 40% will have severe catarrh.

5.2 OPTIMAL EFFECT OF PREVENTIVE TREATMENT

Suppose treatment is given to prevent an individual from developing mild or severe catarrh. That is, the probabilities of making transitions from state 1 to state 2 or state 3 is reduced. This reduction of course depends on the effectiveness of the preventive treatment. The results are summarized in the table below when the treatment is assumed to be 50%, 90% and 99% effective respectively.

Table 6: A summary result of the effective of preventive treatment.

| K | P ₁₁ | P ₁₂ | P ₁₃ |
|----|-----------------|-----------------|-----------------|
| 0 | 0.79 | 0.08 | 0.13 |
| 50 | 0.90 | 0.04 | 0.06 |
| 90 | 0.98 | 0.01 | 0.01 |
| 99 | 1.00 | 0.00 | 0.00 |

It can be seen from the above table that the probabilities of 'no catarrh' increased by 12%, 19%, and 21% respectively when the treatment is assumed to be 50%, 90% and 99% effective respectively.

Conversely, the probabilities of an individual to develop a mild catarrh reduced by about 4%, 7% and 8% respectively when the treatment is assumed to be 50%, 90% and 99% effective respectively.

Similarly, the probability of an individual to develop a severe catarrh has been reduced to 7%, 12% and 13% respectively when the treatment is assumed to be 50%, 90% and 99% effective respectively.

The foregoing analysis shows that it is possible to maximize the probability of an individual not to develop the symptoms of catarrh by 99 percent and at the same time minimize the probability of an individual to develop mild or severe catarrh by at most 99 percent. It is clear from the above table that the probability of an individual having catarrh has been maximized to unity.

Conversely, the probability of developing mild or severe catarrh has been minimized to zero. However, these optimal results are dependent on the effectiveness of the preventive treatment. Hence, collaboration with medical doctors, Pharmacologists, Pharmacists and Nurses is crucial (medical personnel) and must be carried along for effective and optimal prevention of catarrh.

3 THE NON- HOMOGENEOUS CASE

It is possible that the assumption of constant transition probabilities may not be appropriate. In this case, we consider the non- stationary Markov chain.

Suppose the null hypothesis is not accepted at the significance level shown in the previous illustration. The maximum likelihood estimate of the transition probability P_1 and P_2 are as follow:

$$P_1 = \begin{pmatrix} 0.864 & 0.45 & 0.091 \\ 0.133 & 0.600 & 0.267 \\ 0.100 & 0.200 & 0.700 \end{pmatrix}$$

$$P_2 = \begin{pmatrix} 0.706 & 0.118 & 0.176 \\ 0.316 & 0.316 & 0.368 \\ 0.091 & 0.182 & 0.727 \end{pmatrix}$$

$$P = P_1 P_2 = \begin{pmatrix} 0.632 & 0.133 & 0.235 \\ 0.308 & 0.254 & 0.439 \\ 0.197 & 0.202 & 0.600 \end{pmatrix}$$

$$P^2 = \begin{pmatrix} 0.487 & 0.165 & 0.348 \\ 0.359 & 0.194 & 0.447 \\ 0.306 & 0.199 & 0.496 \end{pmatrix}$$

$$P^4 = \begin{pmatrix} 0.403 & 0.182 & 0.416 \\ 0.381 & 0.186 & 0.416 \\ 0.372 & 0.187 & 0.441 \end{pmatrix}$$

$$P^8 = \begin{pmatrix} 0.386 & 0.185 & 0.429 \\ 0.385 & 0.185 & 0.430 \\ 0.385 & 0.185 & 0.431 \end{pmatrix}$$

$$P^{10} = \begin{pmatrix} 0.386 & 0.185 & 0.430 \\ 0.385 & 0.185 & 0.430 \\ 0.386 & 0.185 & 0.430 \end{pmatrix}$$

$$= \begin{pmatrix} 0.39 & 0.19 & 0.43 \\ 0.39 & 0.19 & 0.43 \\ 0.39 & 0.19 & 0.43 \end{pmatrix} \text{corrected to 2 dp}$$

$$\pi_0 = \pi_0 P = (0.39 \ 0.19 \ 0.43)$$

$$\pi_1 = \pi_0 P_1 = (0.40 \ 0.21 \ 0.39)$$

$$\pi_2 = \pi_1 P_2 = (0.39 \ 0.19 \ 0.43)$$

observe that $\pi_0 = \pi_2$ numerically as earlier stated.

It is understood that the severity of catarrh increases from about 39% during wet season to about 43% during the dry season.

Also the probability of not having catarrh reduced from 40% in the wet season to 39% in the dry season. This result confirms the seemly belief that the individual develops catarrh more often in the dry season than in the wet season or vice versa. We observe for the sake of emphasis that this seemly belief has been proved wrong in our earlier result. The algorithm and the computer program in Fortran is presented in the appendix A.

5.4 APPLICATION OF THE CONTINUOUS TIME MARKOV MODEL

The problem of continuous time Markov process is to find the probability that the individual will be in state i at time t given that he was in state j at time t_0 .

The differential equation in matrix form is $\frac{dP(t)}{dt} = P(t)A$ where $P(t)$ is a row vector of state probabilities at time t . To obtain the solution to the above differential equation, the initial condition $P_i(0)$, $i = 1, 2, 3$ must be specified.

The development of the equations that determine the $P_{ij}(t)$ functions for this process can be simplified if the following assumptions are made:

- (1) The process satisfies the Markov property
- (2) The process is stationary
- (3) The probability of a transition from one state to a different state in a short time interval is proportional to Δt .
- (4) The probability of two or more changes of state in a short interval Δt is zero.

We shall consider the transition count matrix of the stationary Markov chain discussed in the previous section

$$M = \begin{pmatrix} 31 & 3 & 8 \\ 8 & 15 & 11 \\ 2 & 4 & 15 \end{pmatrix}$$

Normalizing this matrix using $a_{jj} = -\sum a_{ij}$, we have

$$A = \begin{pmatrix} -8 & 3 & 5 \\ 4 & -15 & 11 \\ 2 & 4 & -6 \end{pmatrix}$$

Thus, the matrix A can be interpreted as the reciprocals of the 'mean times' of the negative exponentially distributed random variable having the cumulative distribution $1 - e^{-\lambda t}$ and mean value $1/\lambda$.

The above matrix indicates that if the individual is in state 1, the time he takes to make a transition to state 3 is exponentially distributed with mean 5 days.

That is to say that if the individual is in state 1, he has a probability $\frac{1}{3} \Delta t$ of making transition to state 2 and a probability of $\frac{1}{5} \Delta t$ making transition to state 3 in the time interval $(t, t + \Delta t)$.

Similarly, if the catarrh patient is in the state 2 he has a probability of $\frac{1}{4} \Delta t$ and probability of $\frac{1}{11} \Delta t$ of making transition to state 1 and state 3 respectively in the interval $(t, t + \Delta t)$

And if the patient is in the state 3, he has probability of $\frac{1}{2} \Delta t$ and a probability of $\frac{1}{4} \Delta t$ of making a transition to state 1 and state 2 respectively in a short interval $(t, t + \Delta t)$.

Table 7: The values of $P_{12}(t)$ for $t = 0, 1, \dots, 12$

| T | $P_{12}(t)$ |
|----|-------------|
| 0 | 0.00000000 |
| 1 | 0.05864984 |
| 2 | 0.14598341 |
| 3 | 0.213049294 |
| 4 | 0.25630439 |
| 5 | 0.28206333 |
| 6 | 0.29674701 |
| 7 | 0.30489939 |
| 8 | 0.30934997 |
| 9 | 0.31175269 |
| 10 | 0.31304009 |
| 11 | 0.313726298 |
| 12 | 0.31409075 |

Table 8: The values of $P_{13}(t)$ for $t = 0, 1, \dots, 12$

| t | $P_{13}(t)$ |
|-----|-------------|
| 0 | 0.00000000 |
| 1 | 0.05235628 |
| 2 | 0.09323153 |
| 3 | 0.11975316 |
| 4 | 0.13559574 |
| 5 | 0.14464284 |
| 6 | 0.14967139 |
| 7 | 0.1524186 |
| 8 | 0.15390246 |
| 9 | 0.15469777 |
| 10 | 0.15512179 |
| 11 | 0.15534703 |
| 12 | 0.15546636 |

These results is as illustrated in figures 8 and 9.

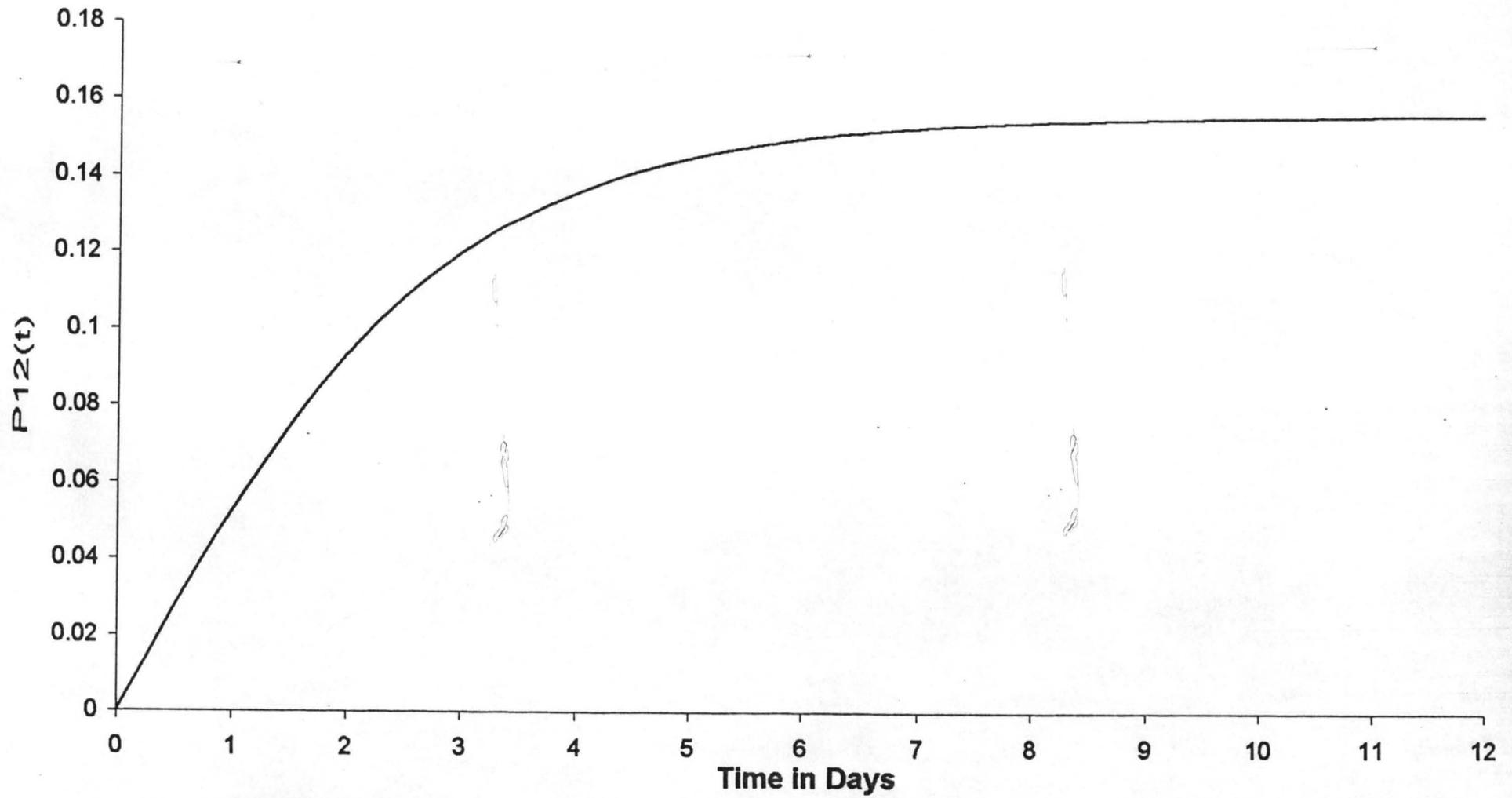


Fig. 8: Graph of $P_{12}(t)$ for $t = 0, 1, \dots, 12$

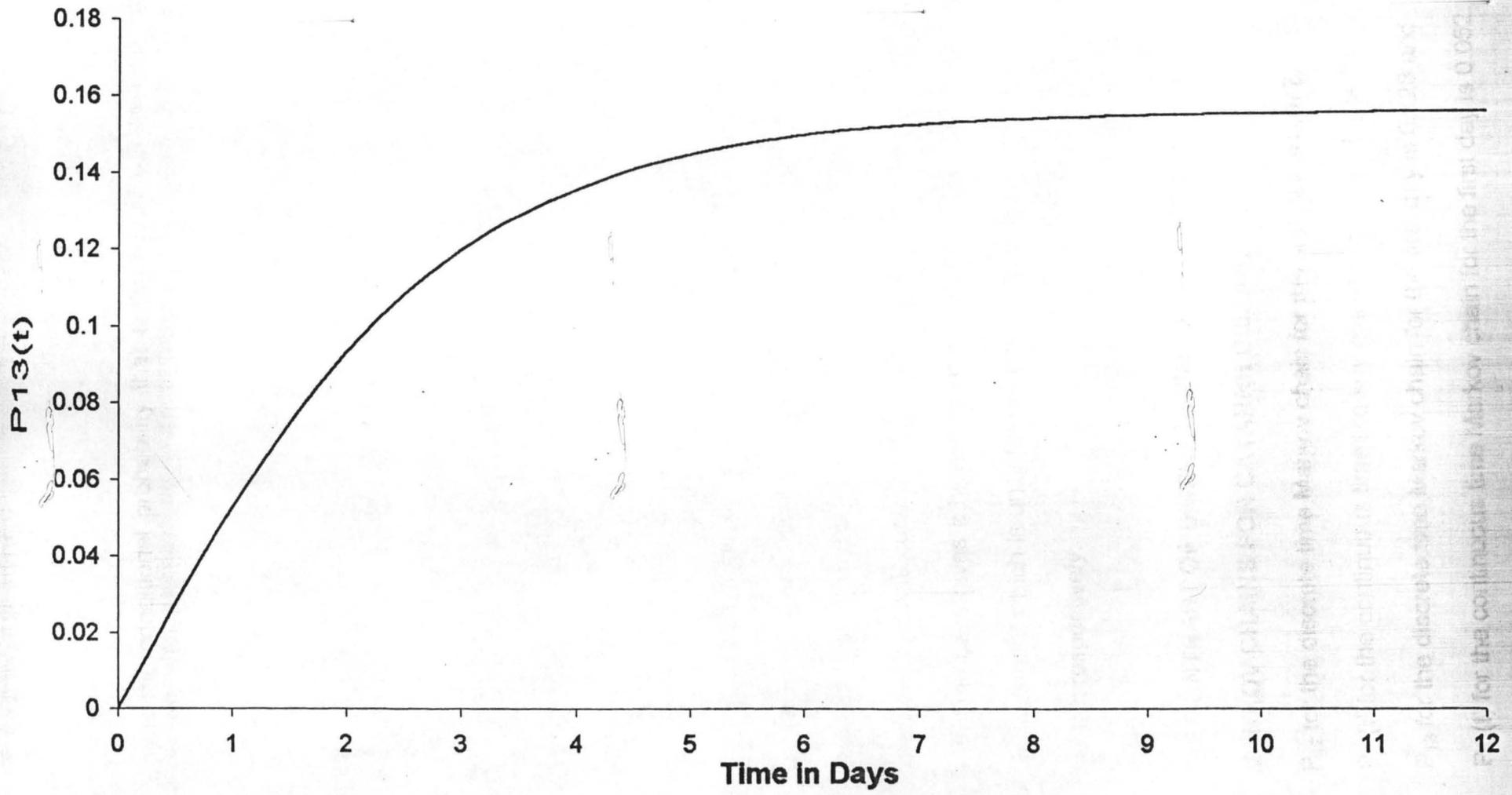


Fig. 9: Graph of $P_{13}(t)$ for $t = 0, 1, \dots, 12$

5.5 COMMENTS

$P_{12}(t)$ is the conditional probability that an individual will develop mild catarrh at time t given that the patient had no symptoms of catarrh at time zero.

$P_{13}(t)$ is the conditional probability that an individual will have a severe catarrh at time t given that the patient has no symptoms of catarrh at time zero.

We have obtained the values for these functions for $t = 0, 1, \dots, 12$ that is, for 12 days since our basic unit of time is a day.

We observe that the limit of each function as t goes to infinity or fairly large is immediately apparent, both in the functions themselves and in the graphs of the functions. The convergence is smooth and monotonic, as opposed to discontinuous, oscillating or both.

$P_{11}(t)$ is the conditional probability that an individual will not have catarrh at time t given that the individual has not symptom of catarrh at time 0. This is the complement of $p_{12}(t)$ and $p_{13}(t)$.

When this result is contrasted with the discrete time case, we see that the discrete time case gives a higher accuracy for the optimal effectiveness of preventive treatment which is unity for not having catarrh and zero for mild and severe catarrh respectively.

5.6 THE CONTRAST OF DISCRETE TIME AND CONTINUOUS TIME MARKOV CHAINS FOR CATARRH DISEASE

P_{12} for the discrete time Markov chain for the first day is 0.077.

$P_{12}(t)$ for the continuous time Markov chain for the first day is 0.059

P_{13} for the discrete time Markov chain for the first day is 0.128 and

$P_{13}(t)$ for the continuous time Markov chain for the first day is 0.052.

We observe that

$$\sum_j p_{ij} = 1 \quad i, j = 1, 2, 3$$

$$\therefore \sum_{j=1}^3 p_{1j} = p_{11} + p_{12} + p_{13}$$

$$= p_{11} + 0.077 + 0.128$$

$$= p_{11} + 0.205$$

$$\therefore p_{11} = 1 - 0.205$$

$$= 0.795$$

Similarly for the continuous time case we have

$$\sum_j P_{ij}(t) = \sum P(x(t) = j | x(0) = i) \quad i, j = 1, 2, 3$$

$$= P(x(t) = \text{Any of its possible states} | x(0) = i) = 1$$

$$\therefore \sum_{j=1}^3 P_{ij}(x(t) = j | x(0) = i)$$

$$= P_{11}(1) + P_{12}(1) + P_{13}(1)$$

$$= P_{11}(1) + 0.059 + 0.052$$

$$= P_{11}(1) + 0.111$$

$$\therefore P_{11}(1) = 1 - 0.111$$

$$= 0.889$$

For $t=1$

From the above analysis, we see that the probability of not having catarrh for the discrete time is 0.795 and for the continuous time is 0.889.

We therefore conclude that the continuous time case provides a higher accuracy than the discrete case. The discrete time converge to 0.41, 0.19 and 0.40 respectively for states 1, 2 and 3 at the sixteenth day or step, whereas the

continuous time stabilised to 0.54, 0.31 and 0.15 respectively for states 1, 2 and 3 at $t = 10$.

5.7 AN ILLUSTRATION OF THE SEMI-MARKOV MODEL

Suppose the following data were collected on a single leprosy patient for 24 years as shown below in table 9.

Table 9: Transition count for leprosy

| | | Actual year | | | | Total |
|-------------------|---------|-------------|---------|---------|---------|-------|
| | | State 1 | State 2 | State 3 | State 4 | |
| Preceding Year | State 1 | 5 | 3 | 2 | 1 | 11 |
| | State 2 | 0 | 3 | 2 | 0 | 5 |
| | State 3 | 4 | 2 | 1 | 0 | 7 |
| | State 4 | 0 | 0 | 0 | 1 | 1 |
| | | | | | | 24 |

The transition probabilities are then estimated from this data using relative frequencies. Thus

$$P = \begin{bmatrix} 0.4 & 0.3 & 0.2 & 0.1 \\ 0 & 0.6 & 0.4 & 0 \\ 0.6 & 0.3 & 0.1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

5.8 EXPONENTIAL HOLDING TIMES IN STATES (DISCRETE)

Suppose that the holding times in each state before making a transition to another state follows the exponential distribution with parameter λ . This implies that the mean holding time in each state is $1/\lambda$ (in years). The mean holding time in each state is shown in table 10.

Table 10: Exponential holding time in states

| Mean holding time | | |
|-------------------|---------|---------|
| State 1 | State 2 | State 3 |
| 3 | 2 | 2 |

The results for the model using these mean holding times are shown in tables 11 - 13 and in figures 10 - 12. Using:

$$\begin{aligned}
 \Phi_{12}(n) &= \sum_{k=1}^4 p_{1k} \sum_{m=1}^n f_{1k}(m) \phi_{k2}(n-m) \\
 &= p_{11} \sum_{m=1}^n f_{11}(m) \phi_{12}(n-m) + p_{12} \sum_{m=1}^n f_{12}(m) \phi_{22}(n-m) + p_{13} \sum_{m=1}^n f_{13}(m) \phi_{32}(n-m) \\
 &\quad + p_{14} \sum_{m=1}^n f_{14}(m) \phi_{14}(n-m) \\
 &= p_{12} \sum_{m=1}^n 0.33e^{-0.33m}
 \end{aligned}$$

Similarly

$$\phi_{13}(n) = p_{13} \sum_{m=1}^n 0.33e^{-0.33m} \quad \text{and}$$

$$\phi_{14}(n) = p_{14} \sum_{m=1}^n 0.33e^{-0.33m}$$

The algorithm, the computer program in Qbasic, and the program output are presented in the appendix C.

Table 11: Interval transition probabilities from state 1 to state 2

| ϕ_{12} | | | |
|-------------|--------------|--------------|--------------|
| n | $K = 0$ | $K = 0.50$ | $K = 0.99$ |
| 1 | 0.0711734593 | 0.1067601815 | 0.1416351795 |
| 2 | 0.1223417446 | 0.1835126132 | 0.2434600741 |
| 3 | 0.1591278315 | 0.2386917472 | 0.3166643977 |
| 4 | 0.1855742335 | 0.2783613503 | 0.3692927361 |
| 5 | 0.2045871764 | 0.3068807721 | 0.4071284831 |
| 6 | 0.2182560414 | 0.3273840547 | 0.4343295097 |
| 7 | 0.2280829102 | 0.3421243429 | 0.4538449890 |
| 8 | 0.2351476699 | 0.3527214825 | 0.4649438472 |
| 9 | 0.2402267000 | 0.3603400290 | 0.4780511260 |
| 10 | 0.2438781261 | 0.3658171892 | 0.4853174686 |
| 11 | 0.2465032190 | 0.3697548509 | 0.4905414283 |
| 12 | 0.2483904809 | 0.3725857139 | 0.4942970574 |

Table 11 presents the interval transition probability from state 1 to state 2. $\phi_{12}(n)$ for $n = 1, 2, 3, \dots, 12$. $\phi_{12}(n)$ is the probability that a leprosy patient will be in state of recovery in year n given that he was under treatment in year zero. In other words, $\phi_{12}(n)$ is the probability of recovery from treatment at time n given that the patient started treatment at time zero.

Table 12: Interval transition probabilities from state 1 to state 3

| n | $\phi_{13}(n)$ | | |
|-----|----------------|--------------|--------------|
| | $K = 0$ | $K = 0.50$ | $K = 0.99$ |
| 1 | 0.0474489704 | 0.0237244852 | 0.0004744892 |
| 2 | 0.0815611631 | 0.0407805815 | 0.0008156108 |
| 3 | 0.1060852185 | 0.0530426092 | 0.0010608512 |
| 4 | 0.1237161532 | 0.0618580766 | 0.0012371604 |
| 5 | 0.1363914460 | 0.0681957230 | 0.0013639132 |
| 6 | 0.1455040276 | 0.0727520138 | 0.0014550389 |
| 7 | 0.1520552635 | 0.0760276318 | 0.0015205512 |
| 8 | 0.1567651033 | 0.0783825517 | 0.0015676495 |
| 9 | 0.1601511240 | 0.0800755620 | 0.0016015097 |
| 10 | 0.1625854224 | 0.0812927112 | 0.0016258527 |
| 11 | 0.1643354744 | 0.0821677372 | 0.0016433533 |
| 12 | 0.1655936539 | 0.0827968270 | 0.0016559350 |

Table 12 shows the interval transition probabilities $\phi_{13}(n)$ for $n = 1, 2, 3, \dots, 12$. $\phi_{13}(n)$ is the probability that a leprosy patient will be a relapse in year n given that the patient was under treatment in year zero. It also represents the probability that a leprosy patient will develop a resistance to the treatment.

Table 13: Interval transition probabilities from state 1 to state 4.

| n | $\phi_{14}(n)$ | | |
|-----|----------------|--------------|--------------|
| | $K = 0$ | $K = 0.50$ | $K = 0.99$ |
| 1 | 0.0237244852 | 0.0118622426 | 0.0002372446 |
| 2 | 0.0407805815 | 0.0203902908 | 0.0004078054 |
| 3 | 0.0530426092 | 0.0265213045 | 0.0005304256 |
| 4 | 0.0618580766 | 0.0309290383 | 0.0006185802 |
| 5 | 0.0681957230 | 0.0340978615 | 0.0006819566 |
| 6 | 0.0727520138 | 0.0363760069 | 0.0007275195 |
| 7 | 0.0760276318 | 0.0380138159 | 0.0007602756 |
| 8 | 0.0783825517 | 0.0391912758 | 0.0007838248 |
| 9 | 0.0800755620 | 0.0400377810 | 0.0008007549 |
| 10 | 0.0812927112 | 0.0406463556 | 0.0008129263 |
| 11 | 0.0821677372 | 0.0410838686 | 0.0008216766 |
| 12 | 0.0827968270 | 0.0413984135 | 0.0008279675 |

Table 13 presents the interval transition probabilities $\phi_{14}(n)$ $n = 1, 2, \dots, 12$. $\phi_{14}(n)$ is the probability that a leprosy patient will die in year n given that the patient was under treatment in year zero.

The above results are illustrated in figures 10 - 12.

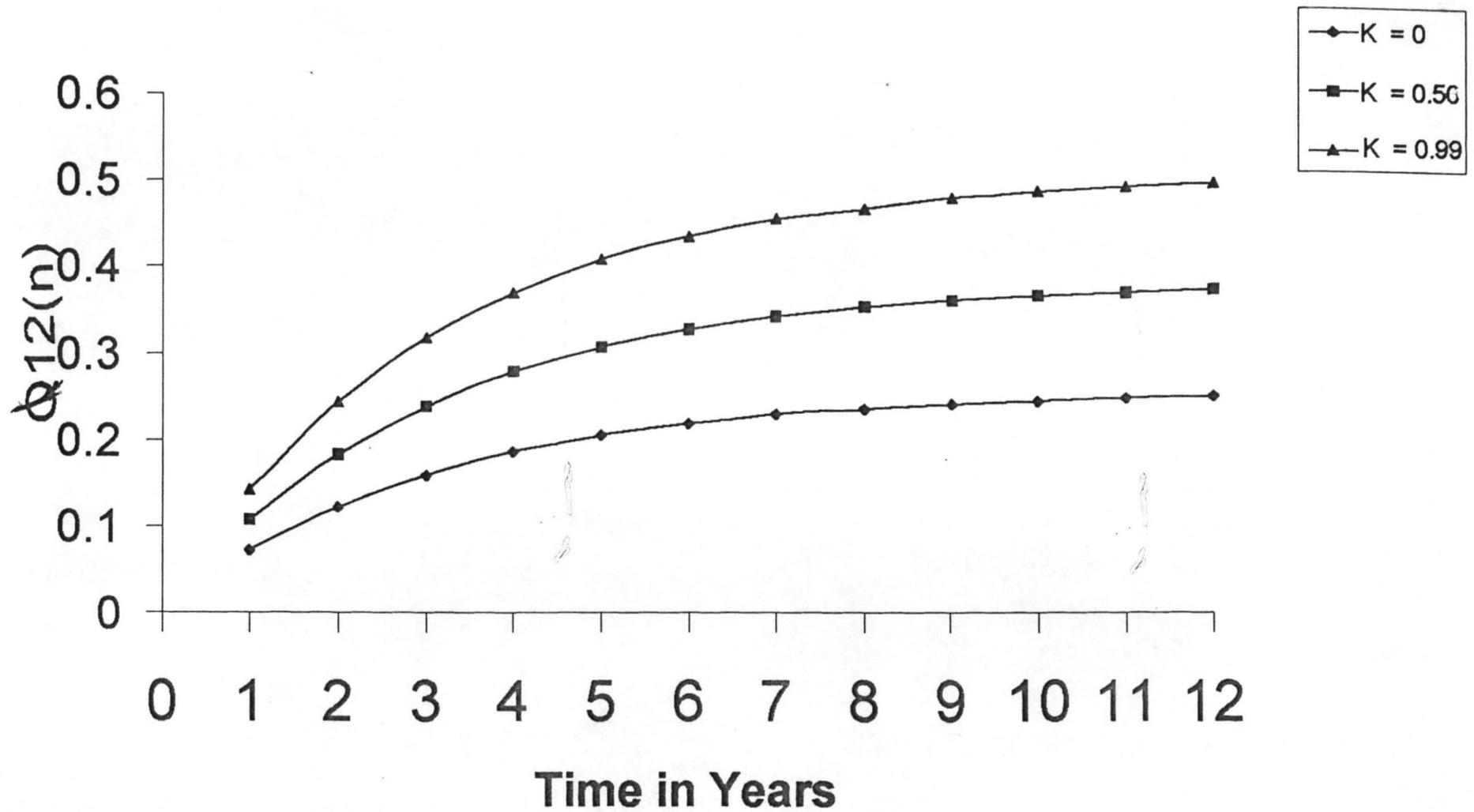


Figure 10: The Graph of interval transition probabilities from state 1 to 2 and the effectiveness of Treatment for exponential distribution in Discrete Time.

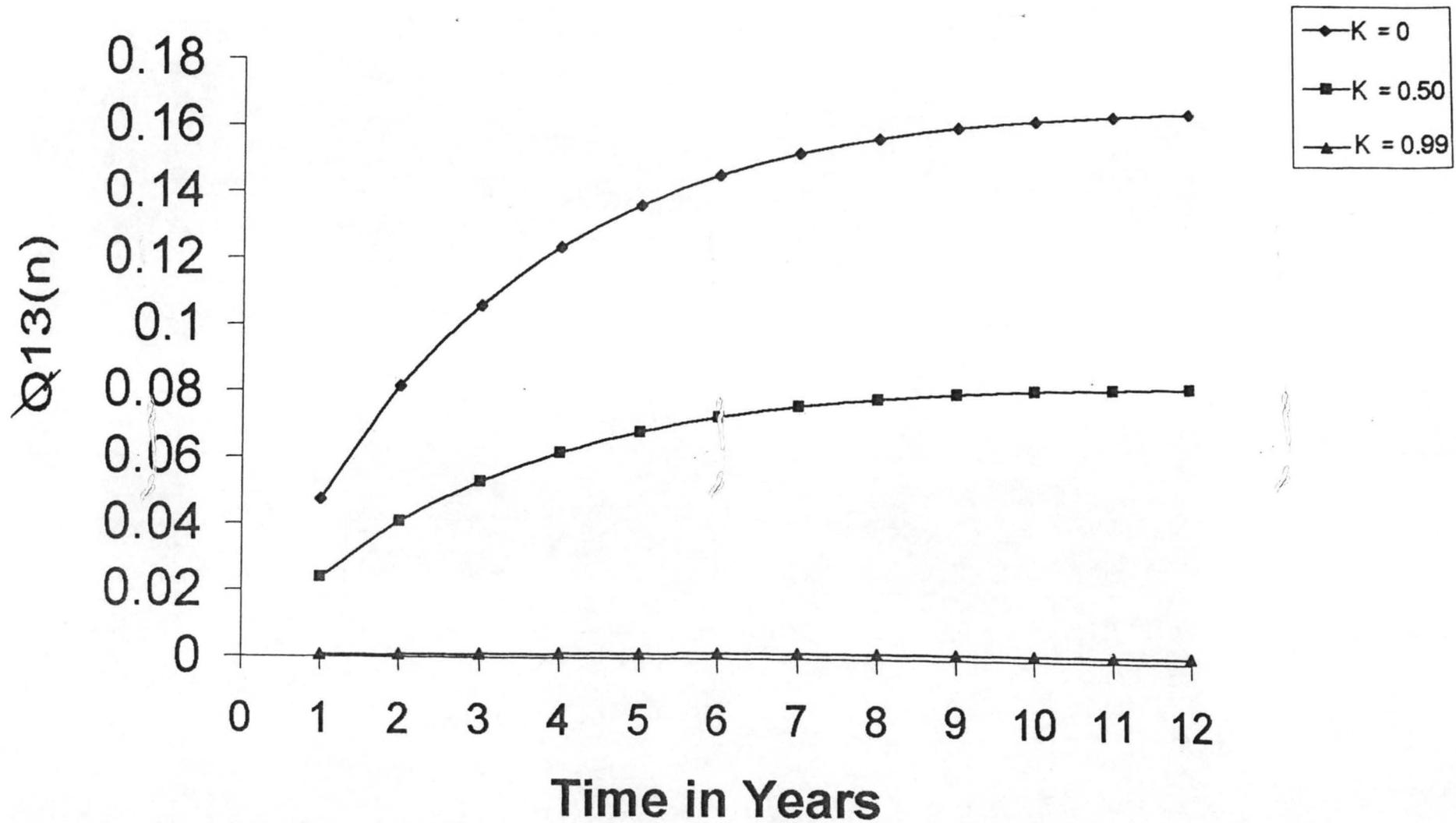


Figure 11: The Graph of interval transition probabilities from state 1 to 3 and the effectiveness of Treatment for exponential distribution in Discrete Time

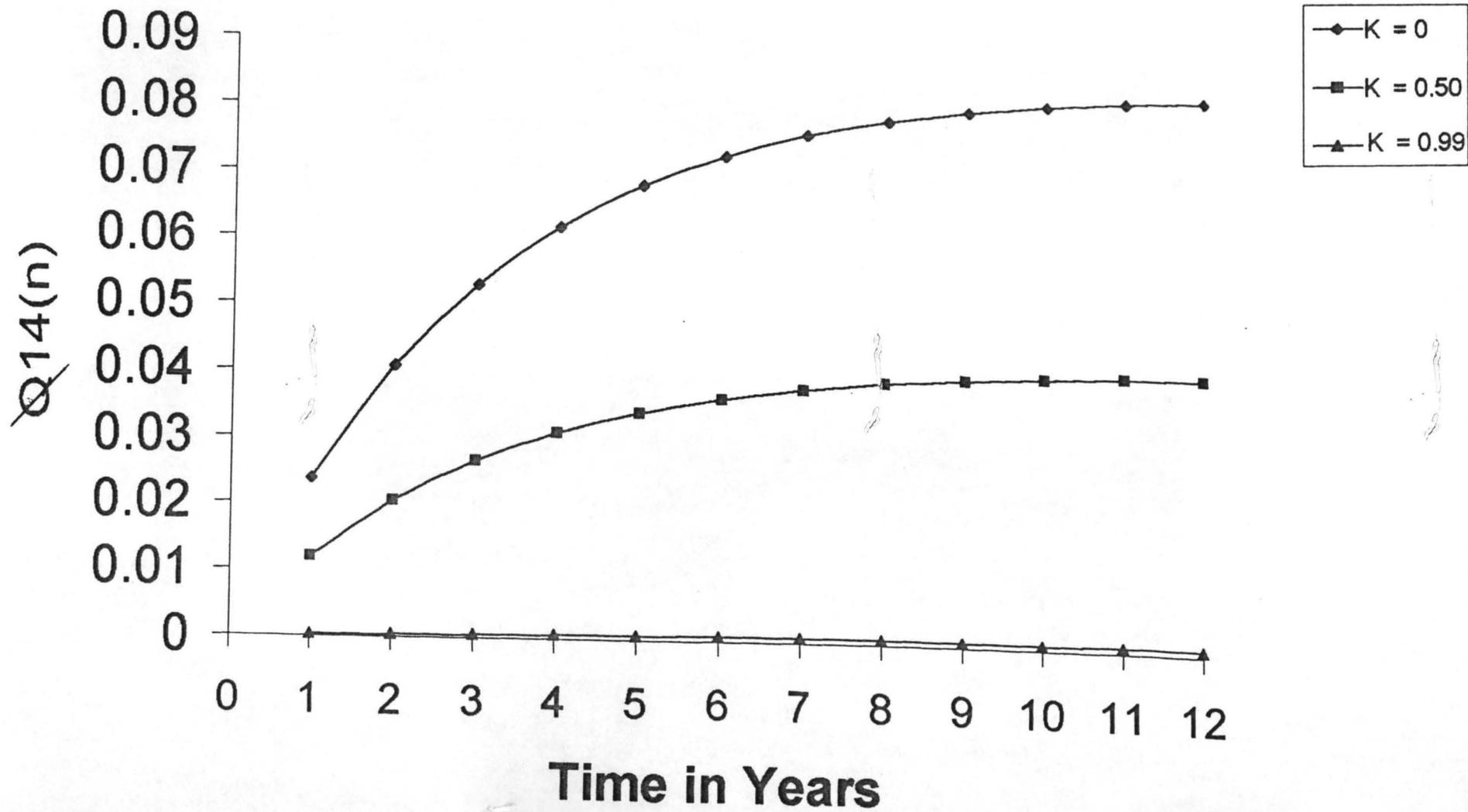


Figure 12: The Graph of $Q_{14}(n)$ vs Time in Years

5.9 WEIBULL HOLDING TIMES IN STATES (DISCRETE)

The results for the model using $\alpha = 10.5$ and $\beta = 1.6$ (see table 3 in page 57) are presented in tables 15-17 and figures 13-15 using:

$$\phi_j(n) = \sum_{j=2}^4 P_{1j} \sum_{m=1}^n 0.152380952(m/10.5)^{0.6} \exp-(m/10.5)^{1.6}$$

Table 14: The interval transition probabilities from state 1 to 2.

| ϕ_{12} | | | |
|-------------|--------------|--------------|--------------|
| n | $K = 0$ | $K = 0.50$ | $K = 0.99$ |
| 1 | 0.0095754713 | 0.0143632062 | 0.0190551877 |
| 2 | 0.0220378209 | 0.0330567323 | 0.0438552648 |
| 3 | 0.0356860533 | 0.0535290837 | 0.0710152462 |
| 4 | 0.0496131815 | 0.0744197667 | 0.0987302288 |
| 5 | 0.0632850900 | 0.0949276388 | 0.1259373277 |
| 6 | 0.0763817355 | 0.1145725995 | 0.1519996524 |
| 7 | 0.0887717359 | 0.1330755502 | 0.1765469015 |
| 8 | 0.1001924053 | 0.1502885967 | 0.1993828863 |
| 9 | 0.1107673943 | 0.1661510915 | 0.2204271257 |
| 10 | 0.1204402894 | 0.1806604415 | 0.2396761775 |
| 11 | 0.1292348504 | 0.1938522607 | 0.2571773529 |
| 12 | 0.1371911019 | 0.2057866454 | 0.2730102837 |

Table 15: The interval transition probabilities from state 1 to 3

$$\phi_{13}(n)$$

| n | $K = 0$ | $K = 0.50$ | $K = 0.99$ |
|-----|--------------|--------------|--------------|
| 1 | 0.0063836472 | 0.0031918236 | 0.0000638364 |
| 2 | 0.0146918809 | 0.0073459405 | 0.0001469187 |
| 3 | 0.0237907022 | 0.0118953511 | 0.0002379068 |
| 4 | 0.0330554519 | 0.0165377259 | 0.0003307542 |
| 5 | 0.0421900600 | 0.0210950300 | 0.0004219002 |
| 6 | 0.0509211533 | 0.0254605766 | 0.0005092110 |
| 7 | 0.0591446869 | 0.0295723435 | 0.0005914463 |
| 8 | 0.0667949319 | 0.0333974659 | 0.0006679487 |
| 9 | 0.0738449320 | 0.0369224660 | 0.0007384486 |
| 10 | 0.0802935287 | 0.0401467644 | 0.0008029345 |
| 11 | 0.0861565620 | 0.0430782810 | 0.0008615648 |
| 12 | 0.0914607272 | 0.0457303636 | 0.0009146064 |

Table 16: The interval transition probabilities from state 1 to 4

| n | $\phi_{14}(n)$ | | |
|-----|----------------|--------------|--------------|
| | $K = 0$ | $K = 0.50$ | $K = 0.99$ |
| 1 | 0.0031918236 | 0.0015959118 | 0.0000319182 |
| 2 | 0.0073459405 | 0.0036729702 | 0.0000734593 |
| 3 | 0.0118953511 | 0.0059476756 | 0.0001189534 |
| 4 | 0.0165377259 | 0.0082688630 | 0.0001653771 |
| 5 | 0.0213950300 | 0.0105475150 | 0.0002109501 |
| 6 | 0.0254605766 | 0.0127302883 | 0.0002546055 |
| 7 | 0.0295723435 | 0.0147861717 | 0.0002957231 |
| 8 | 0.0333974659 | 0.0166987330 | 0.0003339743 |
| 9 | 0.0369224660 | 0.0184612330 | 0.0003692243 |
| 10 | 0.0401467644 | 0.0200733822 | 0.0004014672 |
| 11 | 0.0430782810 | 0.0215591405 | 0.0004307824 |
| 12 | 0.0457303636 | 0.0228651818 | 0.0004573032 |

These results are illustrated in figures 13 - 15.

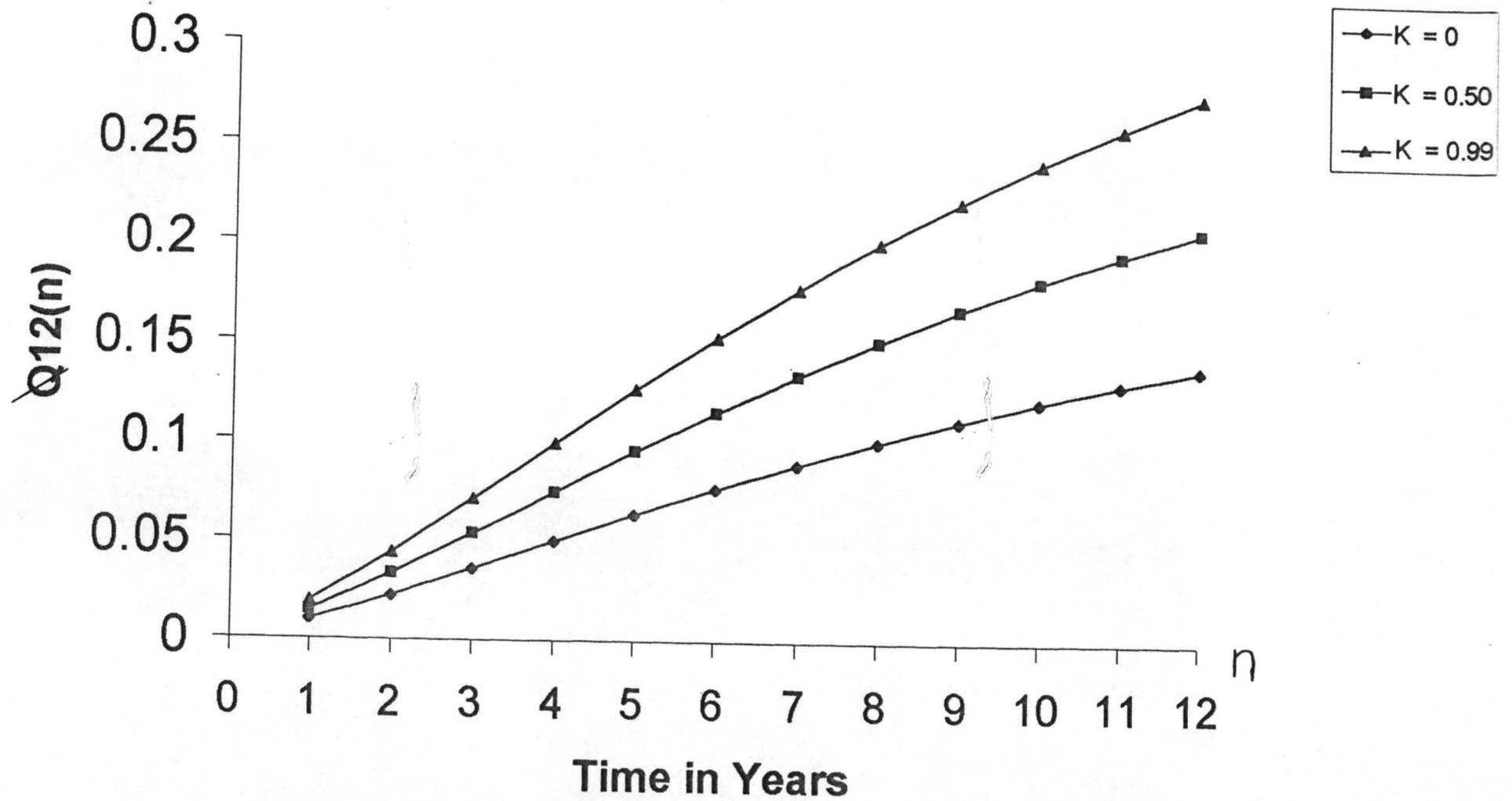


Figure 13: The Graph of interval transition probabilities from state 1 to 2 and the effectiveness of Treatment for Weibull distribution in Discrete Time.

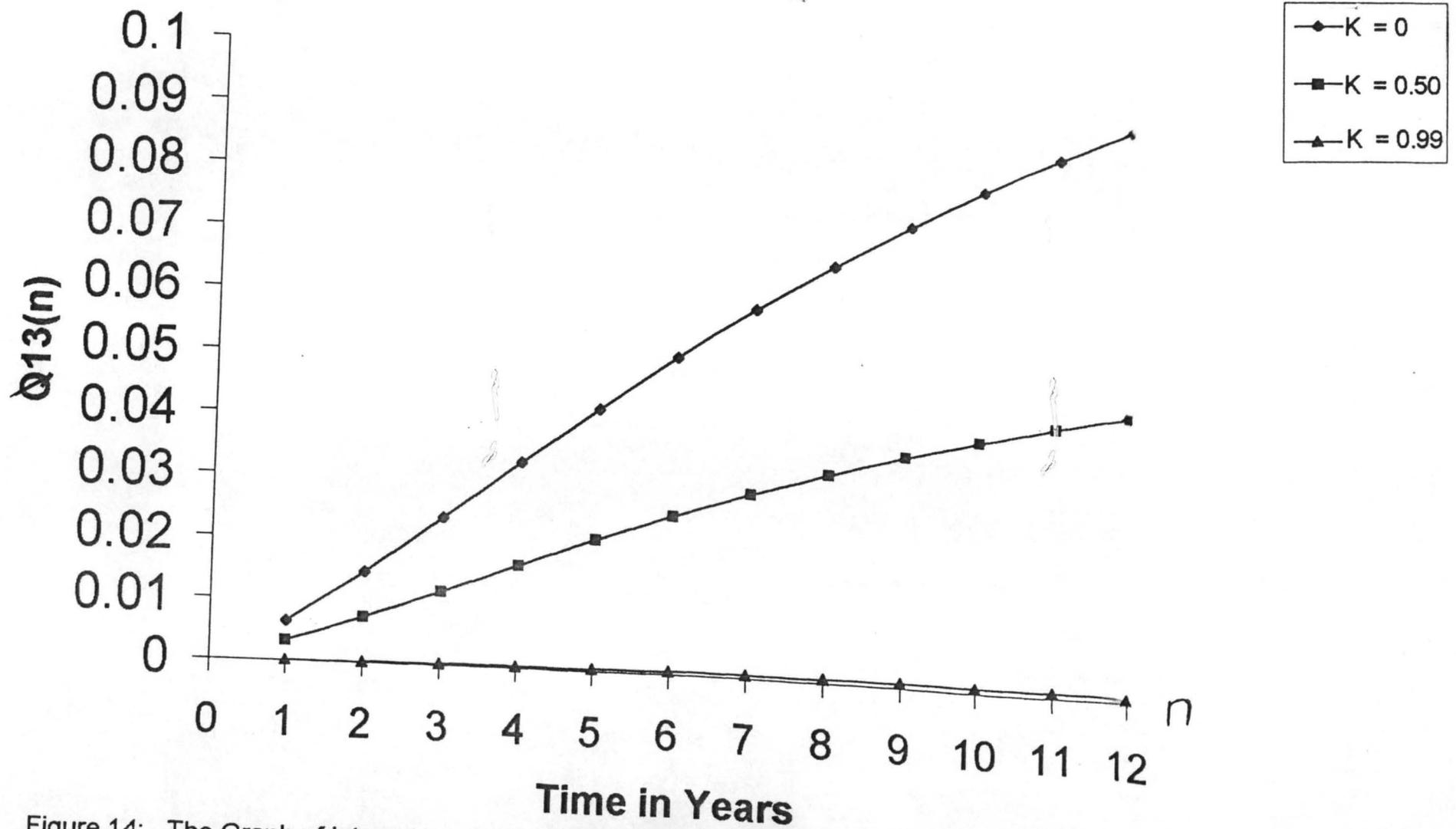


Figure 14: The Graph of interval transition probabilities from state 1 to 3 and the effectiveness of Treatment for Weibull distribution in Disease Time

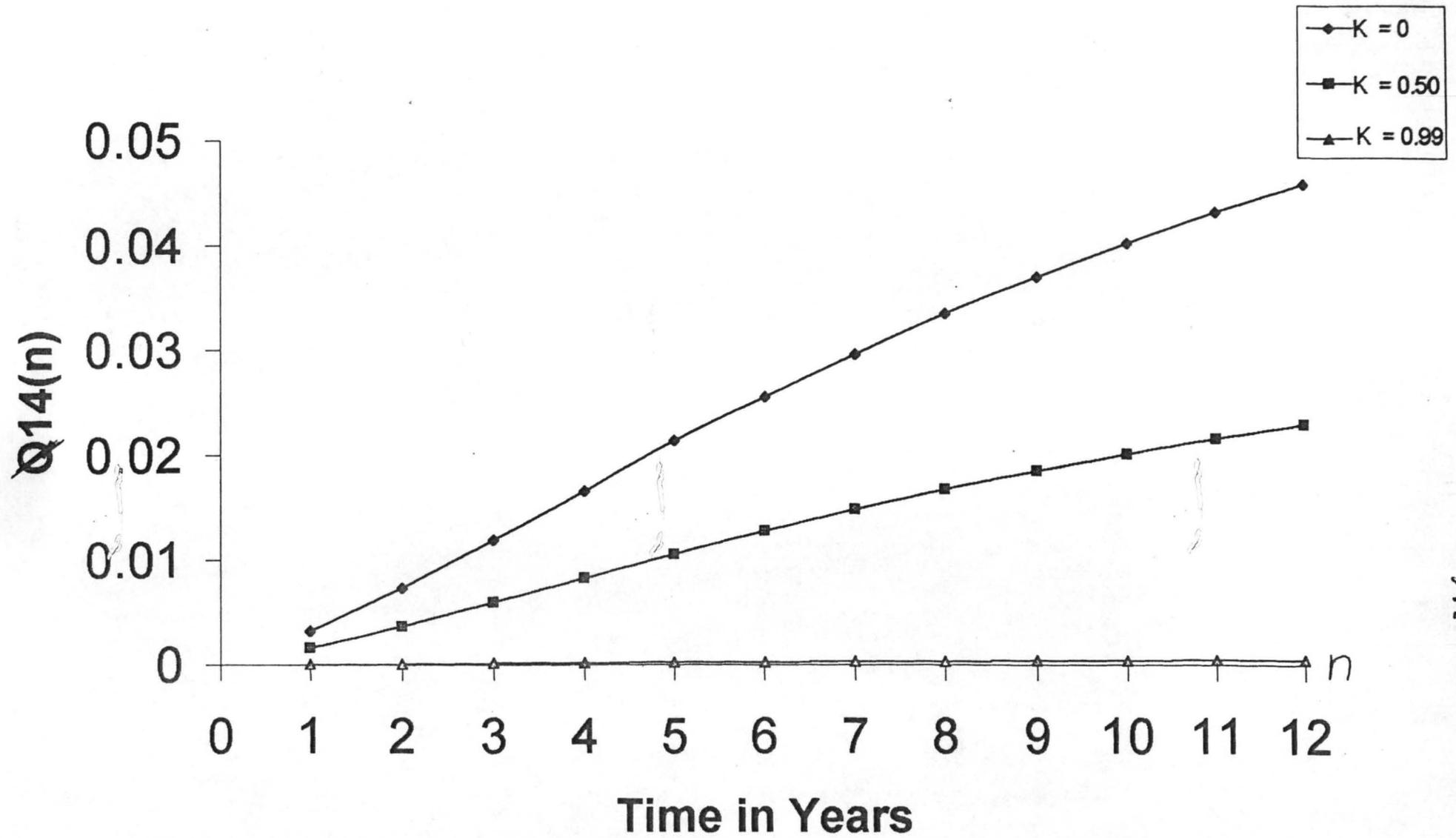


Figure 15: The Graph of interval transition probabilities from state 1 to 4 and the effectiveness of Treatment for Weibull distribution in Discrete Time.

5.10 COMMENTS

The values of the interval transition probabilities $\phi_{ij}^{(n)}$ $j=2,3$ and 4 , $n=0, 1,2 \dots$. Presented in the previous tables shows a low degree of variability in the sensitivity analysis (i.e. the optimal modeling) for both the exponential and Weibull distributions when the time is measured discretely. The behaviour of the probabilities that are evident in the graphs is quite interesting especially in the case of treatment effectiveness.

THE EXPONENTIAL DISTRIBUTION

For the exponential distribution, $\phi_{12}^{(n)}$ increased by about 3% and 7% for the first year. It also increased by about 12% and 24% for the twelfth year when the treatment is about 50% and 99% effective respectively

When the mean holding time in the states is negative exponentially distributed, $\phi_{13}^{(n)}$ for the first year decreased accordingly by 2% and 4%. A corresponding decrease of about 8% and 16% are indicated respectively for the twelfth year period when the treatment is assumed to be 50% and 99% effective

$\phi_{14}^{(n)}$ for the exponential decreased by about 1% and 2% for the first year. It further decreased by about 4% and 8% for the twelfth year period when the treatment is assumed to be 50% and 99% effective.

THE WEIBULL DISTRIBUTION

When the holding time in the state takes Weibull distribution there is little variation (increase) of about 0.4% and 0.9% for the first year for the interval transition probabilities $\phi_{12}^{(n)}$ when the treatment is assumed to be 50% and 99%

effective respectively. However, an increase of about 6% and 13% is obtained for the twelfth year when the treatment is assumed to be 50% and 99% effective respectively.

$\phi_{13}^{(n)}$ was minimized by about 0.3% and 0.6% when the treatment is assumed to be 50% and 99% effective respectively for the first year. For the twelfth year period a minimum of about 5% and 9% is obtained when the treatment is assumed to be 50% and 99% effective.

$\phi_{14}^{(n)}$ for the first year was minimized by about 0.2% and 0.3% respectively when the treatment is assumed to be 50% and 99% effective. This is further minimized by about 2% and 5% respectively for the twelfth year period when the treatment is assumed to be 50% and 99% effective.

5.11 EXPONENTIAL HOLDING TIMES IN STATES (CONTINUOUS TIME)

Here we assume that the holding time in the state follows the exponential distribution shown in previous section:

The interval transition probabilities obtained for the continuous random variables are presented in Tables 18 - 20. Using:

$$\begin{aligned}
 \Phi_{12}(n) &= \sum_{k=1}^4 p_{1k} \int_0^n f_{1k}(m) \Phi_{k2}(n-m) dm \\
 &= p_{11} \int_0^n f_{11}(m) \phi_{12}(n-m) dm + p_{12} \int_0^n f_{12}(m) \phi_{22}(n-m) dm + p_{13} \int_0^n f_{13}(m) \phi_{32}(n-m) dm \\
 &\quad + p_{14} \int_0^n f_{14}(m) \phi_{42}(n-m) dm \\
 &= p_{12} \int_0^n f_{12}(m) \phi_{22}(0) dm = p_{12} \int_0^n f_{12}(m) dm \\
 &= p_{12} \int_0^n 0.33 e^{-0.33m} dm = -p_{12} e^{-0.33m} \Big|_0^n \\
 &= -p_{12} [e^{-0.33n} + e^0] = p_{12} [-e^{-0.33n} + 1]
 \end{aligned}$$

Table 17: Interval transition probability from state 1 to state 2

$$\phi_{12}(n)$$

| n | $K = 0$ | $K = 0.50$ | $K = 0.99$ |
|-----|--------------|--------------|--------------|
| 1 | 0.0843228847 | 0.1264843345 | 0.1678025424 |
| 2 | 0.1449446082 | 0.2174169123 | 0.2884397507 |
| 3 | 0.1885270029 | 0.2827905118 | 0.3751687407 |
| 4 | 0.2198594362 | 0.3297891319 | 0.4375202656 |
| 5 | 0.2423850298 | 0.3635775447 | 0.4823462069 |
| 6 | 0.2585792542 | 0.3878688812 | 0.5145726800 |
| 7 | 0.2702216506 | 0.4053324759 | 0.5377410650 |
| 8 | 0.2785916328 | 0.4178874493 | 0.5543973446 |
| 9 | 0.2846090198 | 0.4269135296 | 0.5663719177 |
| 10 | 0.2889350653 | 0.4334025979 | 0.5749807954 |
| 11 | 0.2920451462 | 0.4380677342 | 0.5811698437 |
| 12 | 0.2942810655 | 0.4414216280 | 0.5856193304 |

Table 17 presents the interval transition probability from state 1 to state 2. $\phi_{12}(n)$ for $n = 1, 2, 3, \dots, 12$. $\phi_{12}(n)$ is the probability that a leprosy patient will be in state of recovery in year n given that he was under treatment in year zero. In other words, $\phi_{12}(n)$ is the probability of recovery from treatment at time n given that the patient started treatment at time zero.

Table 18: Interval transition probabilities from state 1 to state 3

| n | $\phi_{13}(n)$ | | |
|-----|----------------|--------------|--------------|
| | $K = 0$ | $K = 0.50$ | $K = 0.99$ |
| 1 | 0.0562152565 | 0.0281076282 | 0.0005621520 |
| 2 | 0.0966297314 | 0.0483148657 | 0.0009662964 |
| 3 | 0.1256846637 | 0.0628423318 | 0.0012568455 |
| 4 | 0.1465729475 | 0.0732864738 | 0.0014657282 |
| 5 | 0.1615900248 | 0.0807950124 | 0.0016158987 |
| 6 | 0.1723861545 | 0.0861930773 | 0.0017238599 |
| 7 | 0.1801477522 | 0.0900738761 | 0.0018014759 |
| 8 | 0.1857277602 | 0.0928638801 | 0.0018572757 |
| 9 | 0.1897393316 | 0.0948696658 | 0.0018973915 |
| 10 | 0.1926233619 | 0.0963116810 | 0.0019262319 |
| 11 | 0.1946967691 | 0.0973483846 | 0.0019469658 |
| 12 | 0.1961873770 | 0.0980936885 | 0.0019618720 |

Table 18 shows the interval transition probabilities $\phi_{13}(n)$ for $n = 1, 2, 3, \dots, 12$. $\phi_{13}(n)$ is the probability that a leprosy patient will be a relapse in year n given that the patient was under treatment in year zero. It also represents the probability that a leprosy patient will develop a resistance to the drug.

Table 19: Interval transition probabilities from state 1 to state 4.

| n | $\phi_{14}(n)$ | | |
|-----|----------------|--------------|--------------|
| | $K = 0$ | $K = 0.50$ | $K = 0.99$ |
| 1 | 0.0281076282 | 0.0140538141 | 0.0002810760 |
| 2 | 0.0483148657 | 0.0241574328 | 0.0004831482 |
| 3 | 0.0628423318 | 0.0314211659 | 0.0006284228 |
| 4 | 0.0732864738 | 0.0366432369 | 0.0007328641 |
| 5 | 0.0807950124 | 0.0403975062 | 0.0008079493 |
| 6 | 0.0861930773 | 0.0430965386 | 0.0008619300 |
| 7 | 0.0900738761 | 0.0450369380 | 0.0009007379 |
| 8 | 0.0928638801 | 0.0464319400 | 0.0009286379 |
| 9 | 0.0948696658 | 0.0474348329 | 0.0009486958 |
| 10 | 0.0963116810 | 0.0481558405 | 0.0009631159 |
| 11 | 0.0973483846 | 0.0486741923 | 0.0009734829 |
| 12 | 0.0980936885 | 0.0490468442 | 0.0009809360 |

Table 19 presents the interval transition probabilities $\phi_{14}(n)$ $n = 1, 2, \dots, 12$. $\phi_{14}(n)$ is the probability that a leprosy patient will die in year n given that the patient was under treatment in year zero.

The above results are illustrated in figures 16 - 18.

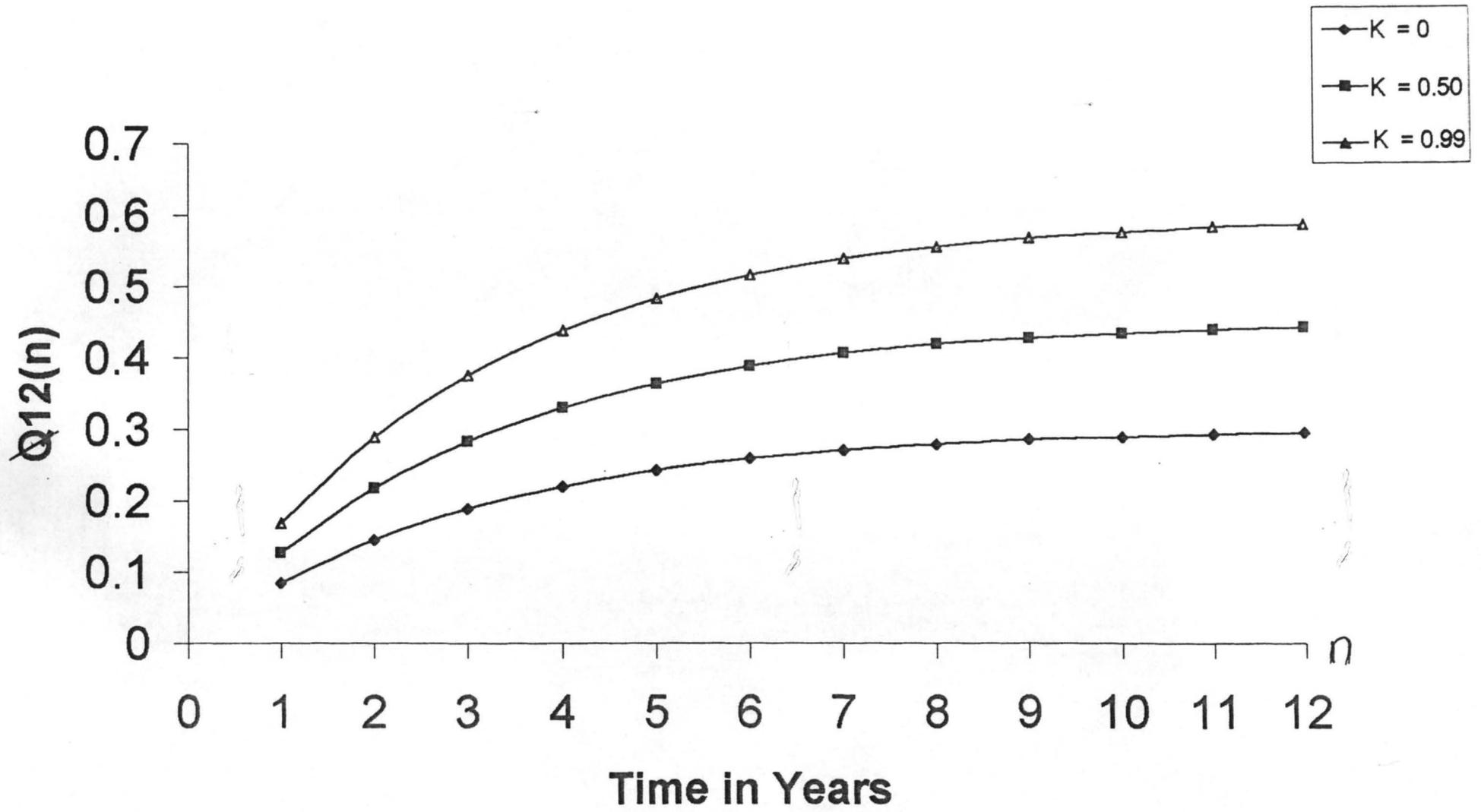


Figure 16: The Graph of interval transition probabilities from state 1 to 2 and the effectiveness of treatment for exponential distribution in Continuous Time.

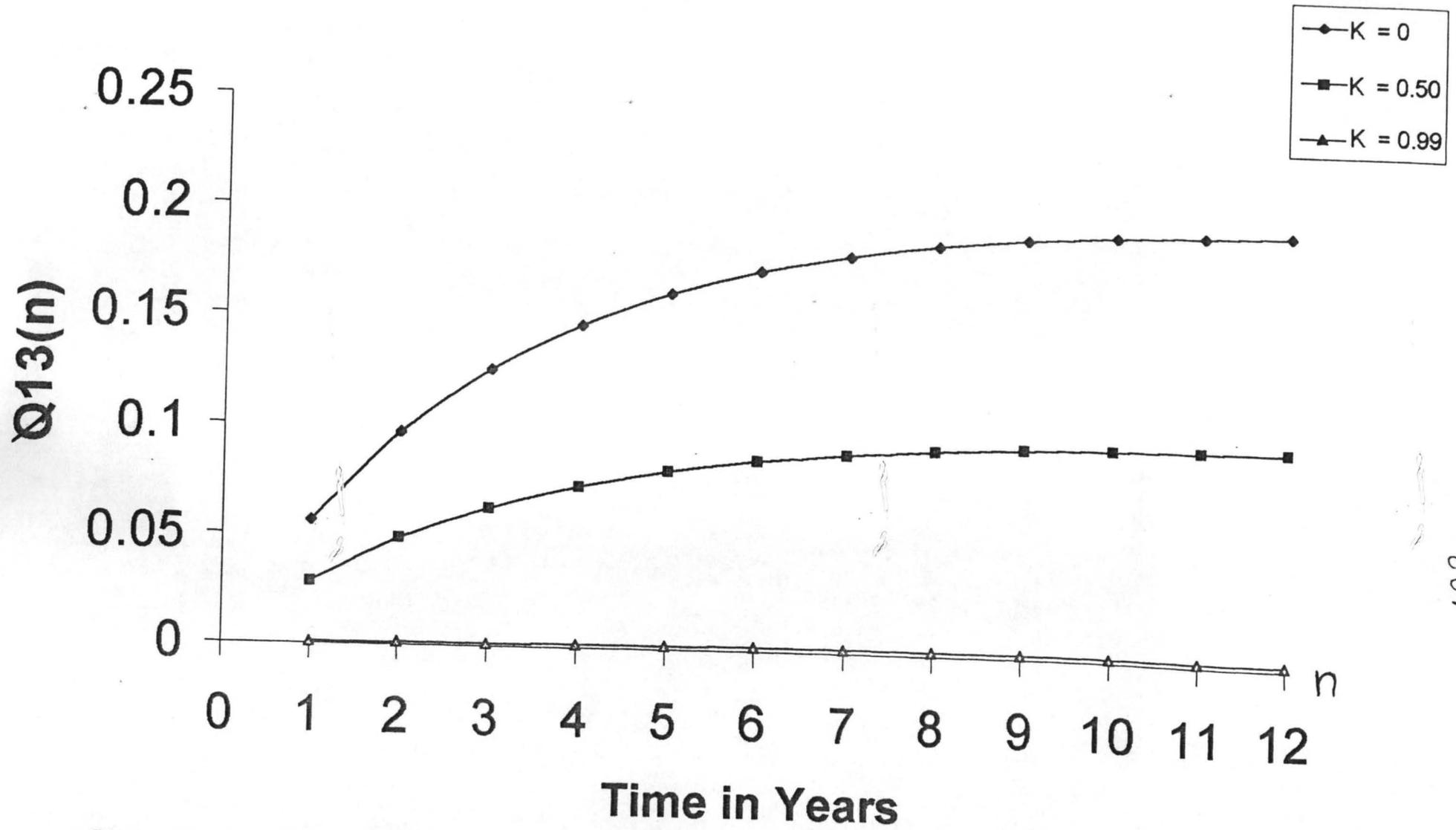


Figure 17: The Graph of interval transition probabilities from state 1 to 3 and the effectiveness of treatment for exponential distribution in Continuous Time.

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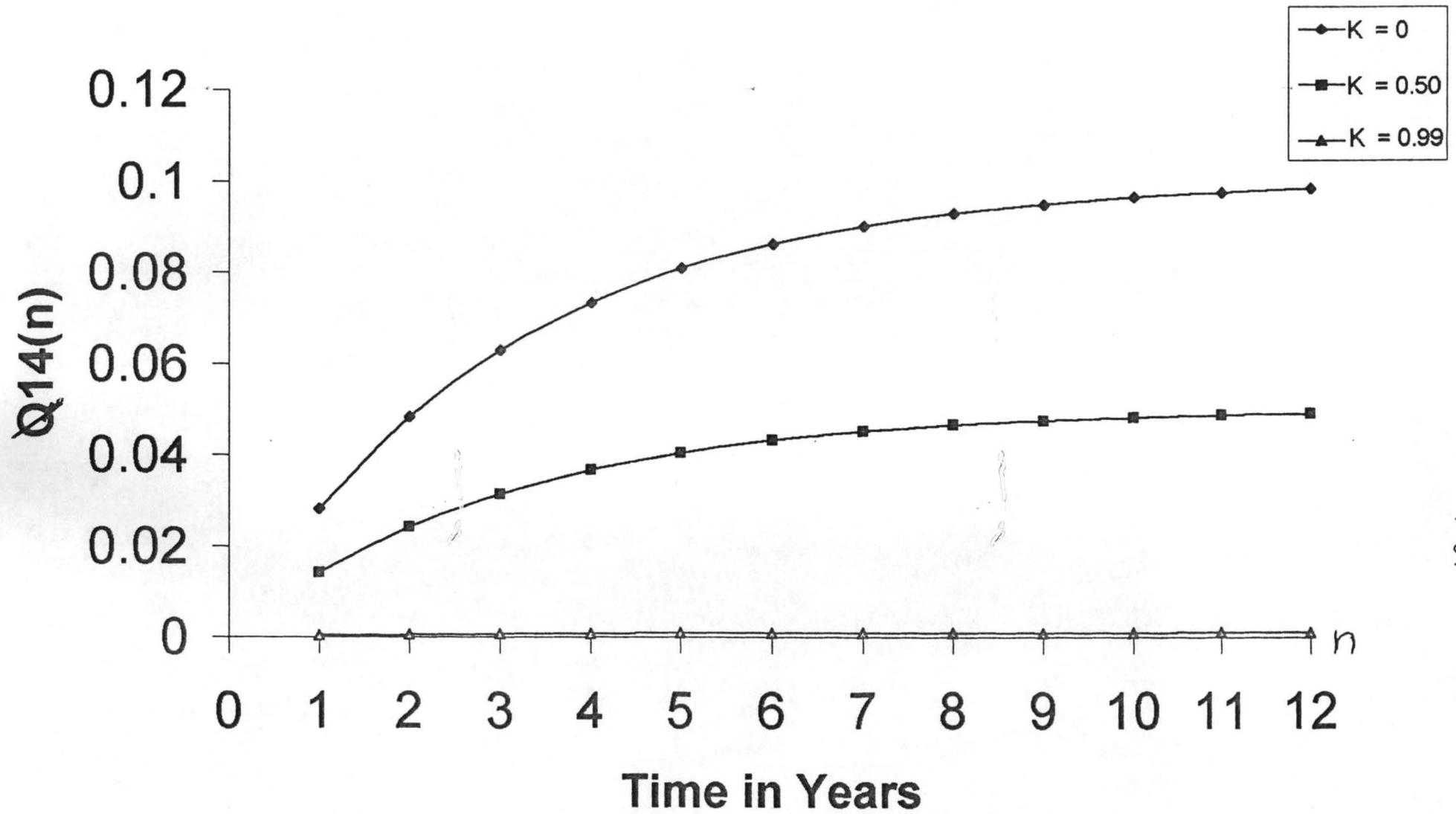


Figure 18: The Graph of interval transition probabilities from state 1 to 4 and the effectiveness of treatment for exponential distribution in Continuous Time.

5.12 WEIBULL HOLDING TIMES IN STATES

Here we assume that the holding time in the state follows the Weibull distribution with parameters α and β . Percentile points are used to estimate the parameters of the distribution as in discrete case.

The interval transition probabilities are presented in Tables 20 – 22 and figures 19-21. Using:

$$\phi_j(n) = p_{1j}(1 - \exp(-(n/10.5)^{1.6}))$$

$$j = 2,3,4.$$

Table 20: The interval transition probabilities from state 1 to 2.

| n | $\phi_{12}^{(n)}$ | | |
|-----|-------------------|--------------|--------------|
| | $K = 0$ | $K = 0.50$ | $K = 0.99$ |
| 1 | 0.0424016714 | 0.0636025071 | 0.0843793303 |
| 2 | 0.0788103342 | 0.1182154939 | 0.1568325609 |
| 3 | 0.1100730374 | 0.1651095450 | 0.2190453410 |
| 4 | 0.1369170994 | 0.2053756565 | 0.2724650204 |
| 5 | 0.1599670649 | 0.2399505824 | 0.3183344603 |
| 6 | 0.1797591746 | 0.2696387470 | 0.3577207625 |
| 7 | 0.1967538744 | 0.2951308191 | 0.3915402293 |
| 8 | 0.2113465667 | 0.3170198500 | 0.4205796719 |
| 9 | 0.2238767594 | 0.3358151317 | 0.4455147386 |
| 10 | 0.2346359193 | 0.3519538641 | 0.4669254720 |
| 11 | 0.2438744158 | 0.3658116162 | 0.4853100777 |
| 12 | 0.2518071532 | 0.3777107298 | 0.5010962486 |

Table 21: The interval transition probabilities from state 1 to 3

| n | $\phi_{13}(n)$ | | |
|-----|----------------|--------------|--------------|
| | $K = 0$ | $K = 0.50$ | $K = 0.99$ |
| 1 | 0.0282677803 | 0.0141338902 | 0.0002826775 |
| 2 | 0.0525402203 | 0.0262701102 | 0.0005254017 |
| 3 | 0.0733820200 | 0.0366910100 | 0.0007338195 |
| 4 | 0.0912780687 | 0.0456390344 | 0.0009127798 |
| 5 | 0.1066447049 | 0.0533223525 | 0.0010664461 |
| 6 | 0.1198394448 | 0.0599197224 | 0.0011983933 |
| 7 | 0.1311692446 | 0.0655846223 | 0.0013116912 |
| 8 | 0.1408977062 | 0.0704488531 | 0.0014089757 |
| 9 | 0.1492511630 | 0.0746255815 | 0.0014925102 |
| 10 | 0.1564239413 | 0.0782119706 | 0.0015642379 |
| 11 | 0.1625829339 | 0.0812914670 | 0.0016258279 |
| 12 | 0.1678714305 | 0.0839357153 | 0.0016787127 |

Table 22: The interval transition probabilities from state 1 to 4

$$\phi_{14}(n)$$

| n | $K = 0$ | $K = 0.50$ | $K = 0.99$ |
|-----|--------------|--------------|--------------|
| 1 | 0.0141338902 | 0.0070669451 | 0.0001413388 |
| 2 | 0.0262701102 | 0.0131350551 | 0.0002627008 |
| 3 | 0.0366910100 | 0.0183455050 | 0.0003669097 |
| 4 | 0.0456390344 | 0.0228195172 | 0.0004563899 |
| 5 | 0.0533223525 | 0.0266611762 | 0.0005332230 |
| 6 | 0.0599197224 | 0.0299598612 | 0.0005991966 |
| 7 | 0.0655846223 | 0.0327923112 | 0.0006558456 |
| 8 | 0.0704488531 | 0.0352244265 | 0.0007044878 |
| 9 | 0.0746255815 | 0.0373127908 | 0.0007462551 |
| 10 | 0.0782119706 | 0.0391059853 | 0.0007821189 |
| 11 | 0.0812914670 | 0.0406457335 | 0.0008129139 |
| 12 | 0.0839357153 | 0.0419678576 | 0.0008393563 |

These results are illustrated in figures 19 - 21.

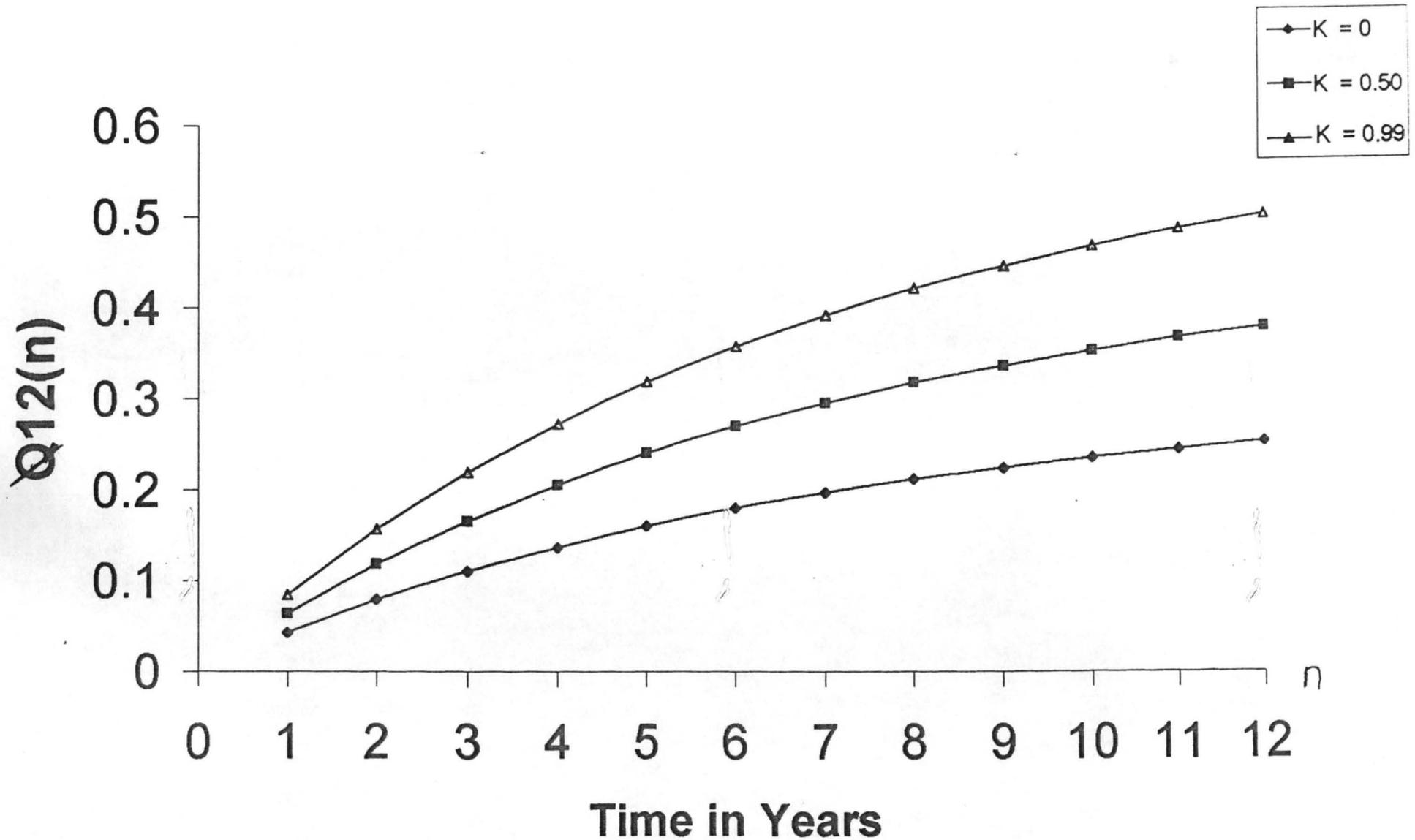


Figure 19: The Graph of interval transition probabilities from state 1 to 2 and the effectiveness of treatment for Weibull distribution in Continuous Time.

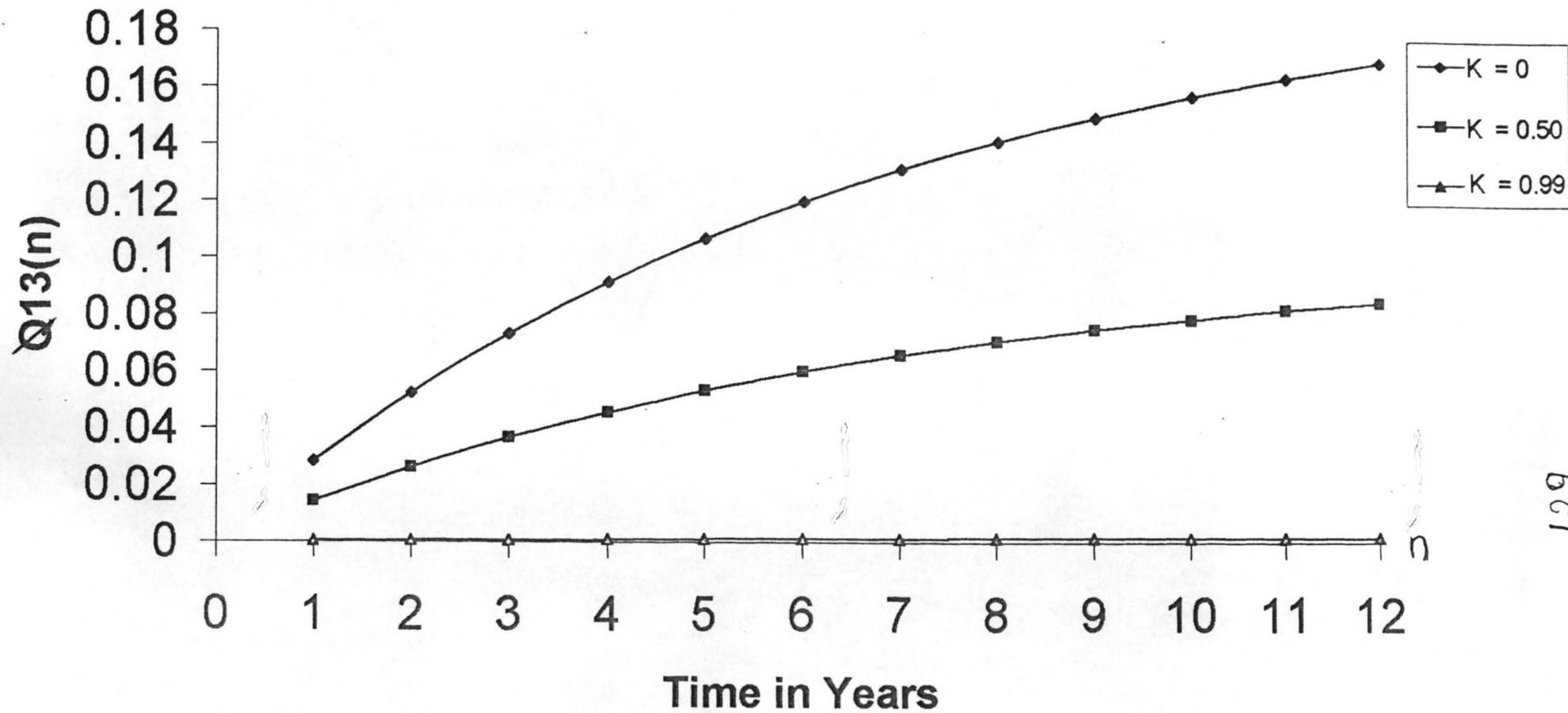


Figure 20: The Graph of interval transition probabilities from state 1 to 3 and the effectiveness of treatment for Weibull distribution in Continuous Time.

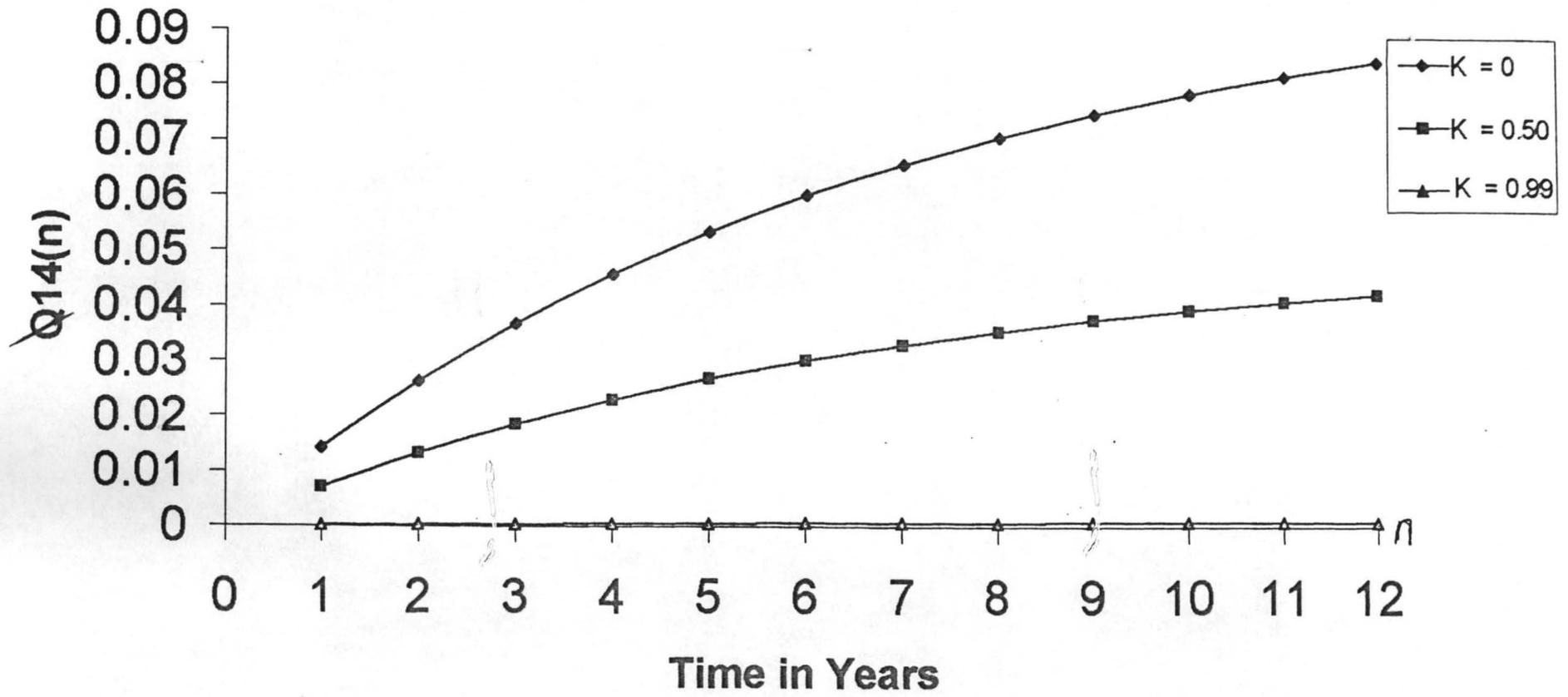


Figure 21: The Graph of interval transition probabilities from state 1 to 4 and the effectiveness of treatment for Weibull distribution in Continuous Time.

5.13 COMMENTS

In the last section we discussed the interval transition probabilities for the exponential and the Weibull distributions when the time is measured discretely. We shall now examine the interval transition probabilities for the same probability distributions but the time is considered on a continuous scale.

EXPONENTIAL DISTRIBUTION

$\phi_{12}^{(n)}$ increased by about 4% and 8% for the first year when the treatment is assumed to be 50% and 99% effective respectively. An increase of about 14% and 29% is obtained for the 12th year period when the treatment is assumed to be 50% and 99% effective respectively.

$\phi_{13}^{(n)}$ on the other hand witnessed a decrease of about 3% and 5% for the first year, about 10% and 19% for the 12th year when the treatment is assumed to be 50% and 99% effective respectively.

Like the $\phi_{13}^{(n)}$, the $\phi_{14}^{(n)}$ is minimized by about 1% and 3% for the first year and about 6% and 10% for the 12th year when the treatment is assumed to be 50% and 99% effective respectively.

WEIBULL DISTRIBUTION

$\phi_{12}^{(n)}$ was maximized by about 2% and 4% for the first year, about 14% and 26% for the 12th year when the treatment is assumed to be 50% and 99% effective respectively.

$\phi_{13}^{(n)}$ was reduced by about 1% and 3% for the first year, about 8% and 17% respectively for the 12th year, when the treatment is assumed to be 50% and 99% effective.

However, a reduction of 3% and 5% for the first year, about 10% and 19% is obtained from the negative exponential distribution. $\phi_{13}^{(n)}$ for the Weibull and continuous time case witnessed a decline of about 1% and 3% for the first year, and about 8% and 17% respectively for the twelfth year when the treatment is assumed to be 50% and 99% effective respectively.

The exponential distribution for the $\phi_{14}^{(n)}$ for the discrete time case reduced by about 1% and 2% for the first year, about 4% and 8% for the twelfth year. The Weibull distribution also has a reduction of about 0.2% and 0.3% for the first year, about 2% and 5% for the twelfth year at 50% and 99% respectively.

For the continuous time case, $\phi_{14}^{(n)}$ is reduced about 1% and 3% for the first year and about 6% and 10% for the twelfth year, when the treatment is assumed to be 50% and 99% effective respectively for the exponential distribution.

$\phi_{14}^{(n)}$ for the Weibull is minimized by about 0.7 and 1% for the first year, about 5% and 9% for the twelfth year respectively when the treatment is assumed to be 50% and 99% effective.

Thus, we conclude that $\phi_{1j}^{(n)}$, $j=2,3$ and 4 have consistent predictive power even at the zero level ($k=0$). This could be explained in terms of low degree of variability for the 50% and 99% treatment effectiveness respectively. These results are summarized in the tables 23, 24 and 25 below.

Table 23

A summary of the Results of the comparison of the Discrete and Continuous Time for the Exponential and the Weibull Distributions: from state 1 to state 2.

| $\phi_{12}(n)$ | | | | | | |
|----------------|---------------------|-----|-----|---------------------|-----|-----|
| Exponential | | | | Weibull | | |
| Time | | 50% | 99% | Time | 50% | 99% |
| Discrete | 1 st yr | 3 | 7 | 1 st yr | 0.4 | 0.9 |
| | 12 th yr | 12 | 24 | 12 th yr | 6 | 13 |
| Continuous | 1 st yr | 4 | 8 | 1 st yr | 2 | 4 |
| | 12 th yr | 14 | 29 | 12 th yr | 14 | 26 |

Table 24

A summary of the Results of the comparison of the Discrete and Continuous Time for the Exponential and the Weibull Distributions: from state 1 to state 3.

| $\phi_{13}(n)$ | | | | | | |
|----------------|---------------------|-----|-----|---------------------|-----|-----|
| Exponential | | | | Weibull | | |
| Time | | 50% | 99% | Time | 50% | 99% |
| Discrete | 1 st yr | 2 | 4 | 1 st yr | 0.3 | 0.6 |
| | 12 th yr | 8 | 16 | 12 th yr | 5 | 9 |
| Continuous | 1 st yr | 3 | 5 | 1 st yr | 1 | 3 |
| | 12 th yr | 10 | 19 | 12 th yr | 8 | 17 |

Table 25

A summary of the Results of the comparison of the Discrete and Continuous Time for the Exponential and the Weibull Distributions: from state 1 to state 4.

| $\phi_{14}(n)$ | | | | | | |
|----------------|---------------------|-----|-----|---------------------|-----|-----|
| Exponential | | | | Weibull | | |
| Time | | 50% | 99% | Time | 50% | 99% |
| Discrete | 1 st yr | 1 | 2 | 1 st yr | 0.2 | 0.3 |
| | 12 th yr | 4 | 8 | 12 th yr | 2 | 5 |
| Continuous | 1 st yr | 1 | 3 | 1 st yr | 0.7 | 1 |
| | 12 th yr | 6 | 10 | 12 th yr | 5 | 9 |

5.15 AN ILLUSTRATION OF THE MARKOV-MULTIDRUGS DECISION PROCESS FOR THE CONTROL OF DISEASES

In this section, we shall provide the numerical illustration for the Markov-Multidrug decision algorithm discussed in the last chapter.

We shall consider the stationary transition probabilities for catarrh disease discussed in chapter three.

$$P = \begin{bmatrix} 0.795 & 0.077 & 0.128 \\ 0.235 & 0.441 & 0.324 \\ 0.095 & 0.190 & 0.714 \end{bmatrix} = \begin{bmatrix} 0.8 & 0.1 & 0.1 \\ 0.2 & 0.5 & 0.3 \\ 0.1 & 0.2 & 0.7 \end{bmatrix} \text{ to } I_d p$$

Suppose that

$$R = \begin{bmatrix} 0 & 1 & 3 \\ 2 & 3 & 4 \\ 1 & 2 & 4 \end{bmatrix} \text{ in } \mathbb{N} \text{ 100 is the corresponding rewards (costs) to the transition}$$

matrix P.

We also suppose that when the patient is in state 1 the two alternatives open to him/her are:

Alternative1: Self-medication/ cares

Alternative2: Go to see a doctor

Let the corresponding transition probabilities and rewards (costs) be given as

$$({}^1P_{11} \ {}^1P_{12} \ {}^1P_{13}) = (0.6 \ 0.2 \ 0.2)$$

$$({}^1R_{11} \ {}^1R_{12} \ {}^1R_{13}) = (1 \ 1 \ 3)$$

And

$$({}^2P_{11} \ {}^2P_{12} \ {}^2P_{13}) = (0.8 \ 0.1 \ 0.1)$$

$$({}^2R_{11} \ {}^2R_{12} \ {}^2R_{13}) = (1 \ 2 \ 2)$$

When the patient is in state 2, the two alternatives open to him/her are:

Alternative 1: low priced drugs

Alternative 2: high priced drugs

Let the corresponding transition probabilities and cost be given as

$$({}^1P_{21} \ {}^1P_{22} \ {}^1P_{23}) = (0.1 \ 0.6 \ 0.3)$$

$$({}^1R_{21} \ {}^1R_{22} \ {}^1R_{23}) = (2 \ 2 \ 3)$$

And

$$({}^2P_{21} \ {}^2P_{22} \ {}^2P_{23}) = (0.6 \ 0.3 \ 0.1)$$

$$({}^2R_{21} \ {}^2R_{22} \ {}^2R_{23}) = (3 \ 2 \ 4)$$

When the patient is in state 3, the two alternatives open to him/her are:

Alternative 1: continue without change of drugs

Alternative 2: change drugs

Let the corresponding transition probabilities and reward be given as

$$({}^1P_{31} \ {}^1P_{32} \ {}^1P_{33}) = (0.1 \ 0.2 \ 0.7)$$

$$({}^1R_{31} \ {}^1R_{32} \ {}^1R_{33}) = (1 \ 2 \ 4)$$

And

$$({}^2P_{31} \ {}^2P_{32} \ {}^2P_{33}) = (0.5 \ 0.4 \ 0.1)$$

$$({}^2R_{31} \ {}^2R_{32} \ {}^2R_{233}) = (3 \ 2 \ 1)$$

We shall use these values to determine the best policies for every n.

Using

$${}^0V_i^{(n)} = \min_{k \in D} \left[{}^k\phi_i + \sum_{j=1}^3 {}^k\rho_{ij} {}^0V_j^{(n-1)} \right] \quad n = 1, 2, 3, 4, 5 \text{ and } i = 1, 2, 3, \quad k = 1, 2$$

$$\text{where } {}^k\phi_i = \sum_{j=1}^3 {}^k\rho_{ij} {}^kR_{ij}$$

For n = 1, we have

$$1\phi_1 = {}^1P_{11}{}^1R_{11} + {}^1P_{12}{}^1R_{12} + {}^1P_{13}{}^1R_{13}$$

$$= 0.6 * 1 + 0.2 * 3 = 1.4$$

$$1\phi_2 = {}^1P_{21}{}^1R_{21} + {}^1P_{22}{}^1R_{22} + {}^1P_{23}{}^1R_{23}$$

$$= 0.1 * 2 + 0.6 * 2 + 0.3 * 3 = 2.3$$

$$1\phi_3 = {}^1P_{31}{}^1R_{31} + {}^1P_{32}{}^1R_{32} + {}^1P_{33}{}^1R_{33}$$

$$= 0.1 * 1 + 0.2 * 2 + 0.7 * 4 = 3.3$$

$$2\phi_1 = {}^2P_{11}{}^2R_{11} + {}^2P_{12}{}^2R_{12} + {}^2P_{13}{}^2R_{13}$$

$$= 0.8 * 1 + 0.1 * 2 + 0.1 * 2 = 1.2$$

$$2\phi_2 = {}^2P_{21}{}^2R_{21} + {}^2P_{22}{}^2R_{22} + {}^2P_{23}{}^2R_{23}$$

$$= 0.6 * 3 + 0.3 * 2 + 0.1 * 4 = 2.8$$

$$2\phi_3 = {}^2P_{31}{}^2R_{31} + {}^2P_{32}{}^2R_{32} + {}^2P_{33}{}^2R_{33}$$

$$= 0.5 * 3 + 0.4 * 2 + 0.1 * 1 = 2.4$$

And hence we have

$$d_1^{(1)} = 2, \quad d_2^{(1)} = 1, \quad d_3^{(1)} = 2 \text{ with}$$

$${}^0V_1^{(1)} = 1.2, \quad {}^0V_2^{(1)} = 2.3 \text{ and } {}^0V_3^{(1)} = 2.4$$

The continuation of this computational procedure is contained in appendix D.

The summary of the results is presented below:

TABLE 26: A Summary result of the Optimal Policies and Costs

| N | $d_1^{(n)}$ | $d_2^{(n)}$ | $d_3^{(n)}$ | ${}^0V_1^{(n)}$ | ${}^0V_2^{(n)}$ | ${}^0V_3^{(n)}$ |
|----------|-------------|-------------|-------------|-----------------|-----------------|-----------------|
| 1 | 2 | 1 | 2 | 1,200 | 2,300 | 2,400 |
| 2 | 2 | 2 | 2 | 2,850 | 4,450 | 4,160 |
| 3 | | 2 | 2 | 4,340 | 6,260 | 6,020 |
| 4 | 2 | 2 | 2 | 5,900 | 7,880 | 7,680 |
| 5 | 2 | 2 | 2 | 7,480 | 9,470 | 9,270 |
| | 2 | | | | | |

5.16 COMMENTS

The fore-going results indicate the best policies for every n . $d_i^{(n)}$ where $n = 1, 2, 3, 4, 5$ and $i = 1, 2, 3$. n represents the time; in the case of catarrh model the time frame is a day and for the leprosy model the time is a year.

$d_i^{(n)}$ represents the best policy for each state i at time n . Thus, we have obtained the best policies for the three states in five days for the catarrh models and five years for the leprosy models.

In addition to the best policies, the corresponding expected total minimum costs are also provided. For instance, $d_1^{(1)} = 2$ with ${}^0V_1^{(1)} = 1.2$ means that the best policy for state 1 for the first day/year is to see the doctor and the corresponding expected total cost is one hundred and twenty Naira (₦120.00)

We can see from the results that except for the $d_2^{(1)} = 1$ with ${}^0V_2^{(1)} = 2.3$ the best policy for others is 2. Which means that the best policy for every other state and time is the 'Alternative 2'. This is a kind of convergence to a stable

policy. This type of convergence is not generally true of this iterative algorithm as earlier mentioned. However, it adds some beauty to this result.

We have earlier indicated that this algorithm despite its weakness for non-convergence for a large n ; it is appropriate in our case for the following reason(s).

The iterations signify time and usually the treatment of catarrh disease takes at most 7 days depending on the type of drugs. If recovery is not achieved, the patient has to be referred for laboratory test for some other diseases.

In the case of leprosy disease, the treatment is in average of 5 years. It again depends on the types of drugs.

In view of the above analysis, we see that 5 to 7 time units for the iteration is small and reasonable.

CHAPTER SIX

6.0 CONCLUSION, SUMMARY AND SUGGESTIONS FOR FURTHER STUDY

6.1 CONCLUSION

The results obtained from these models are as follows:

- 1) The three state models for catarrh disease indicates from the available data that catarrh disease does not depend on the season. The implication of this result on the part of microbiologists is that the influenza virus grows and spreads evenly in the two seasons. On the medical point of view drugs for the treatment of catarrh should be readily available throughout the seasons.
- 2) Although the result is as stated in (1) above, it is possible to obtain a contrary result hypothetically as provided for in the model.
- 3) One other important result of the catarrh and leprosy models is the determination of the preventive treatment and curative treatment on the sensitivity analysis. The result indicates that:
 - (i) It is possible to attain 99% preventive treatment to the individual not to develop catarrh disease.
 - (ii) It is also possible by 99% to maximize the recovery of leprosy patient from the disease.
 - (iii) It is at the same time possible at the percentage to minimize relapse or death due to leprosy.

- 4) The comparison of the results obtained for the leprosy model for the discrete time and continuous time shows that the latter provides higher values. Thus for a greater accuracy the continuous time model should be adopted. A similar result was also obtained for the Markov chain model for catarrh.
- 5) When the Weibull and the exponential distributions are contrasted we observed that basically they provide the same result both for the continuous and the discrete time units. We therefore conclude that either one of them is sufficient for the distribution function of the holding time in the disease states
- 6) The leprosy model enables us to establish quantitatively the level of control of leprosy in the near and far future on the basis of the present level of control. This is the basis of Markov process, given the present; future is independent of the past. This result is of great importance to the government and non-governmental organisations that are involved in the eradication of leprosy disease.
- 7) We have been able also to determine the optimal costs of control of the disease using Markov decision processes. Thus, we conclude that it is 'cheaper' to visit a medical doctor and make use of 'high priced' drugs instead of self-care and 'cheap drugs' respectively.

6.2 SUMMARY

In chapter one, we presented the research problem(s) thus: the existing models do not help us to predict the future control of leprosy based on current level of control and whether the catarrh disease is seasonal. The significance of the study includes; the models are predictive tools for studying the progression of the catarrh and leprosy diseases. The results are important information to the patients, government and non-governmental organizations that are concerned about the control of these diseases/eradication of leprosy in 5-12 years.

We also gave brief formal definitions and theory of stochastic processes; a family of a random variables indexed by a time parameter is called a stochastic process.

Markov processes form a subclass of stochastic process with highly simplified dependence assumptions and a wide range of applications including recovery, relapse and death due to diseases.

Depending on the nature of the state space and the parameter space, we could divide Markov processes into four classes. When the parameter and state space are discrete, the Markov process is called a Markov chain. Otherwise the process is simply referred to as a Markov process.

A semi-Markov process is a stochastic process in which the changes of state occur according to a Markov chain and for which the time interval between two successive transitions is a random variable whose distribution may depend on the state from which the transition takes place.

The influenza virus causes catarrh, otherwise known as common cold. The period of incubation is from 24 hours to 48 hours. The treatment involves the application of Nasal decongestants, antibiotics and analgesic.

Leprosy is defined as a chronic infectious disease primarily of the skin and nerves caused by 'mycobacterium leprae'. It is one of the least infectious of all the infectious diseases. The incubation period varies from less than a year to several years with an average of three to five years. The two main types are the tuberculoid and the lepromatous. Leprosy is widely distributed in the tropical and sub-tropical regions. Leprosy can be treated and cured even without the associated deformities, if it is discovered and treated early.

The exponential and Weibull distributions have been discussed as they relate to duration of stay in a state. They have been used for the distributions of holding times in the state. The relative advantage of exponential is that, it is specified by one parameter and can be easily estimated. It has property of 'memoryless'. It is a special case of the Weibull distribution. The relative advantage of the Weibull distribution is that it provides an increasing function for the hazard or failure rate. The percentile points have been used to estimate the two parameters of the Weibull distribution.

We see that the modeling for the control of diseases started as far back as the ancient Greeks with the epidemic of Hippocrates (459-377BC).

Deterministic and stochastic models were developed in the early part of the 20th century. The deterministic perspective is the one in which a change in the independent factor x results in a change in the value of the dependent y , leading to a mathematical function of some kind. In the stochastic models, probability theory and statistical techniques are used to access evidence

regarding causality. In causal analysis of data, the goal is to account for variation in the dependent variable.

It was observed that mathematical formulations on the epidemiology of leprosy are not new. In several occasions, models have been used to study the transmission and spread of leprosy side by side with the past prevalence and incidence of new cases.

We presented a three state model for the catarrh disease. The model provides for the stationary Markov chain and the non-stationary (Non-homogeneous). The result obtained from the Markov chain indicates that catarrh disease does not depend on the season of the year. On the basis of this stationary process of catarrh we further considered the model for discrete states and continuous time. This will enable us to obtain information about the catarrh disease at any given point in time. These models provide illustrations for the optimal level of the effectiveness of the preventive treatment.

A semi-Markov model is presented. We considered leprosy as a disease where the transition of people from one state of the disease to another may not occur at discrete time instants. We therefore look at a situation where the time between transitions can depend on state from which or to which the transition is being made. This leads to one form of Markov process called the semi-Markov process. In other words we have considered the leprosy disease as a semi-Markov process running in discrete and continuous times. The semi-Markov process requires input data such as the transition probability of the Markov chain and mean holding time in the state. Four distinct and mutually exclusive states were specified for the process. The model was considered for discrete state and discrete time and also for discrete state and continuous time.

It is in the literature that the exponential and Weibull distributions are the only candidates for holding time in the state Howard (1960). It is on this basis that we make use of the two functions for the sake of comparison. We observed that the two distribution functions produce the similar results. We contrasted the discrete and continuous time and we observed that the continuous time gave higher values for the interval transition probabilities. The semi-Markov model can be used as a predictive device for studying the health status of leprosy the patients. The predictions will be useful to doctors, hospital administrators, policy makers and the general public.

The successful use of these models developed here would require joint work by the medical personnel and applied mathematicians. The problem of communication between these two groups of people is greatly reduced by not using advanced mathematics.

6.3 SUGGESTIONS FOR FURTHER STUDIES

Three seasons (the wet season, cold-dry season and hot-dry season) could be considered for the catarrh model instead of the two overlapping seasons proposed by Iloeje (1981). The leprosy model could be more realistic if the following conditions were considered: The state of recovery (state 2) could be an absorbing state so that the patient that does not develop a relapse gets absorbed and recovered from the disease forever since leprosy can be treated and cured. Also, many leprosy patients could be studied using this model. These could be basis for further research.

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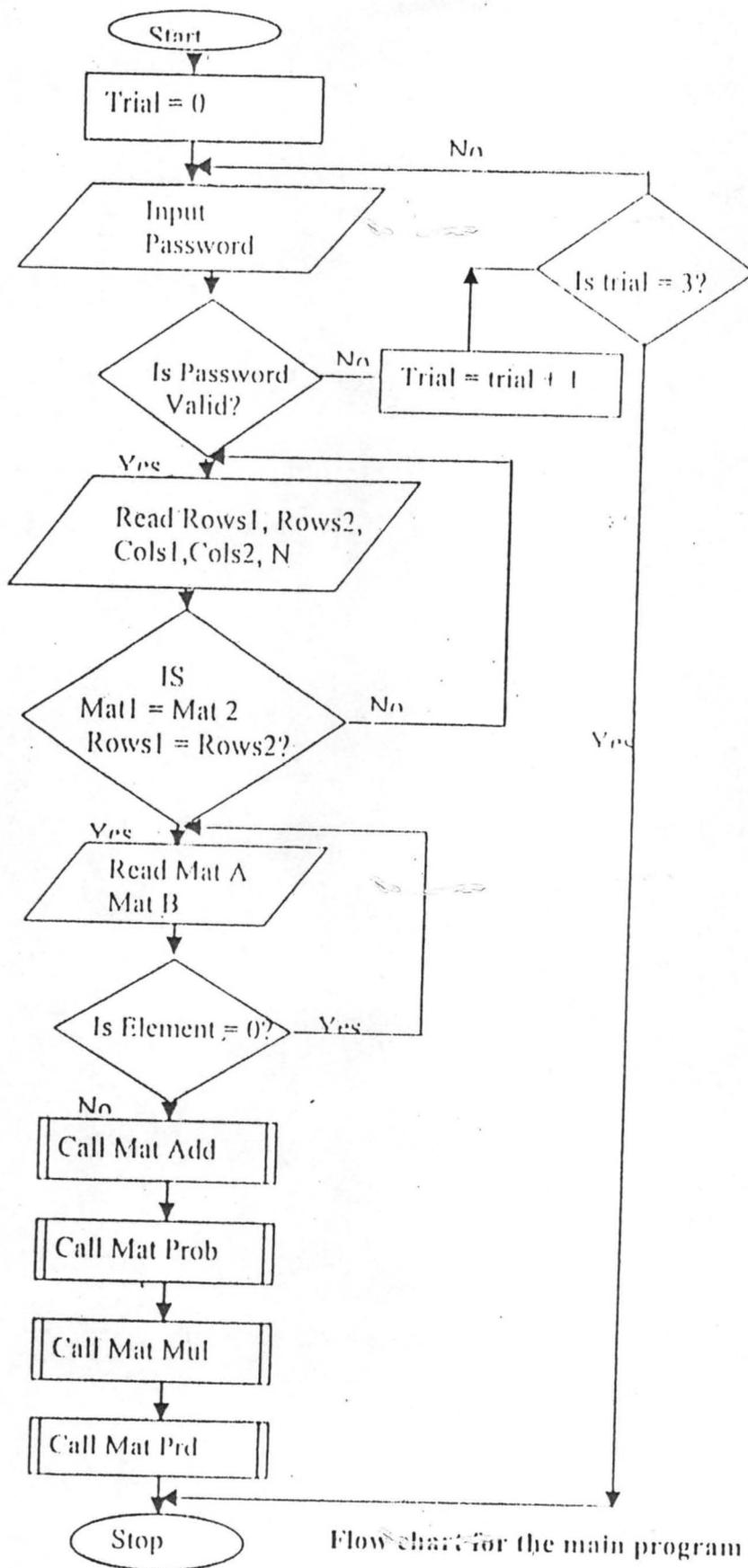
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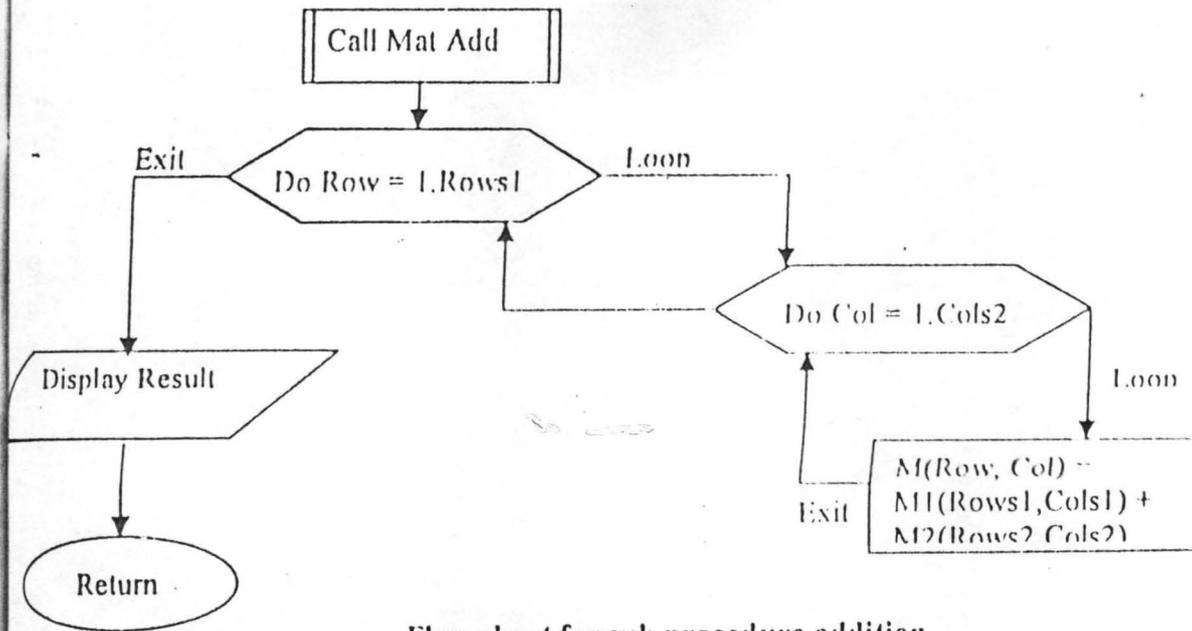
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APPENDIX A

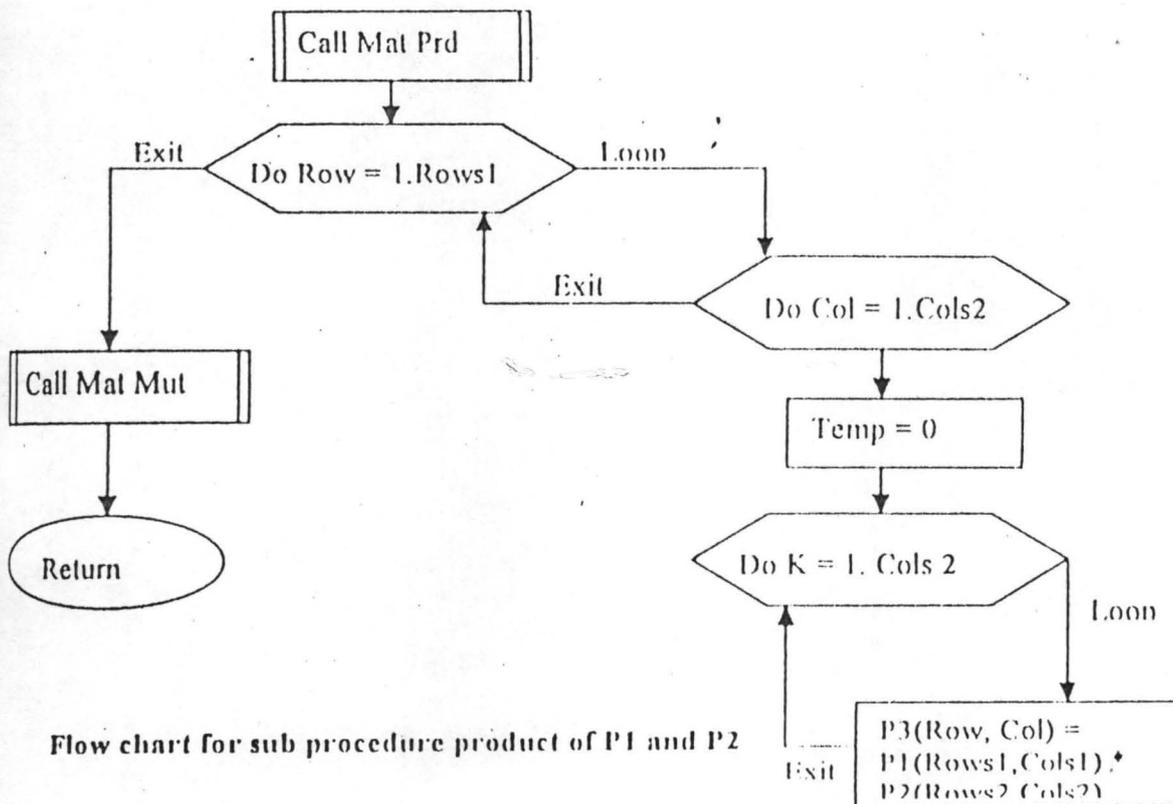
The following is the algorithm presented in the flowcharts, and the computer programs in the FORTRAN language for the Markov chain (discrete state and time) model for Catarrh disease.



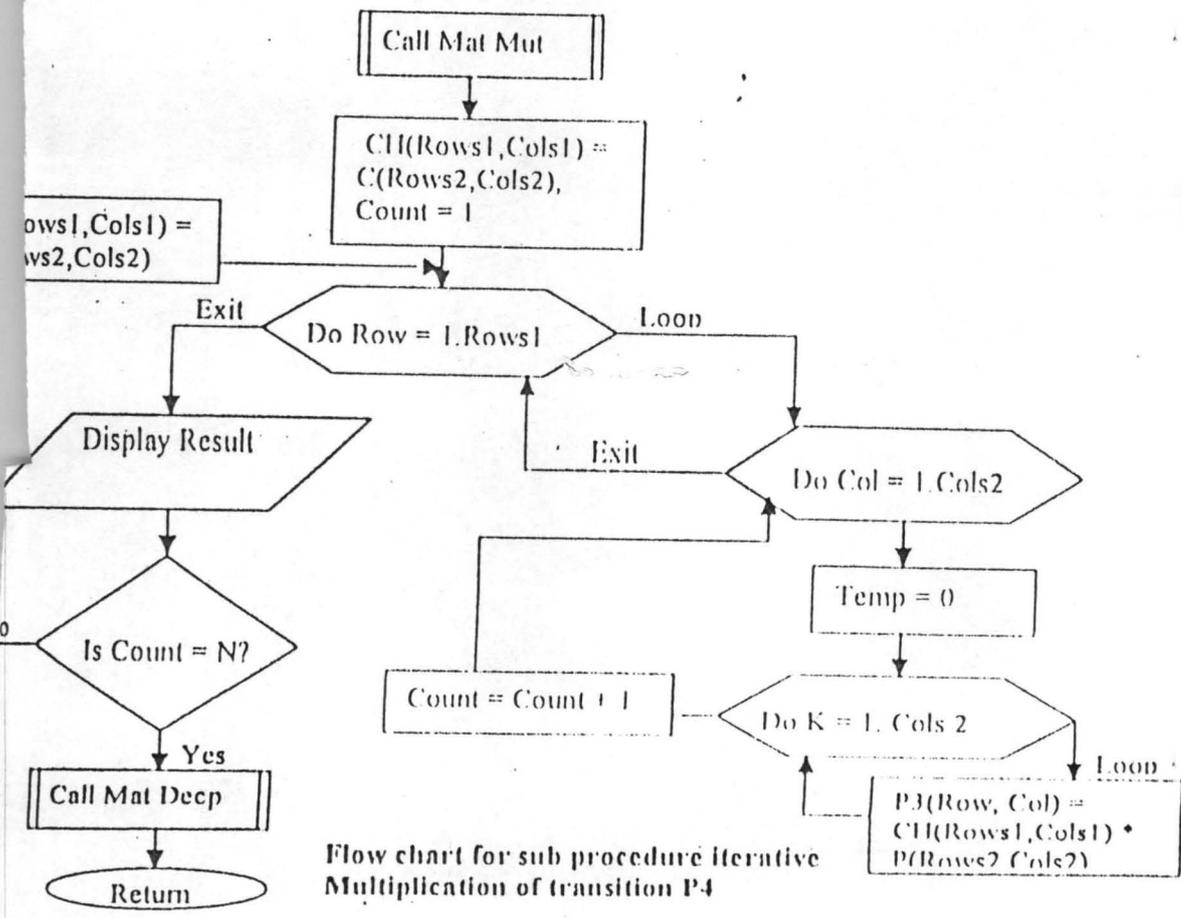
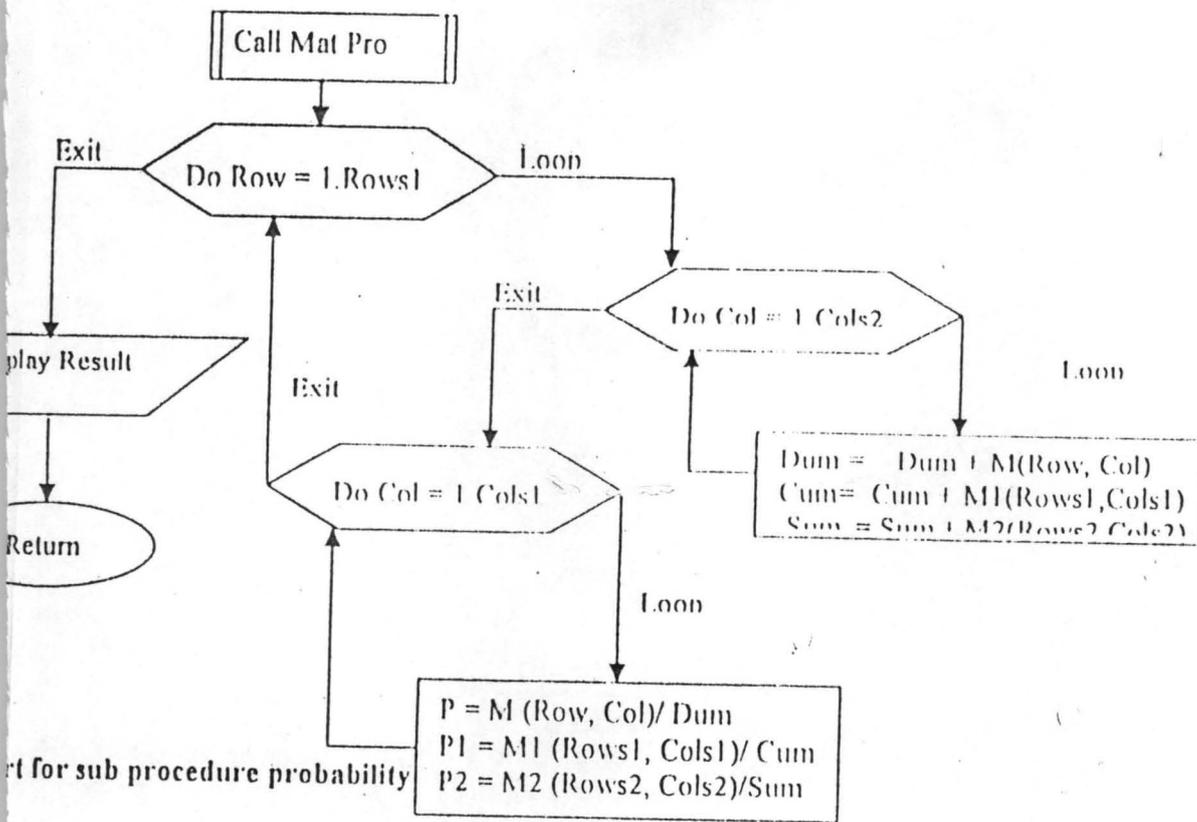
Flow chart for the main program



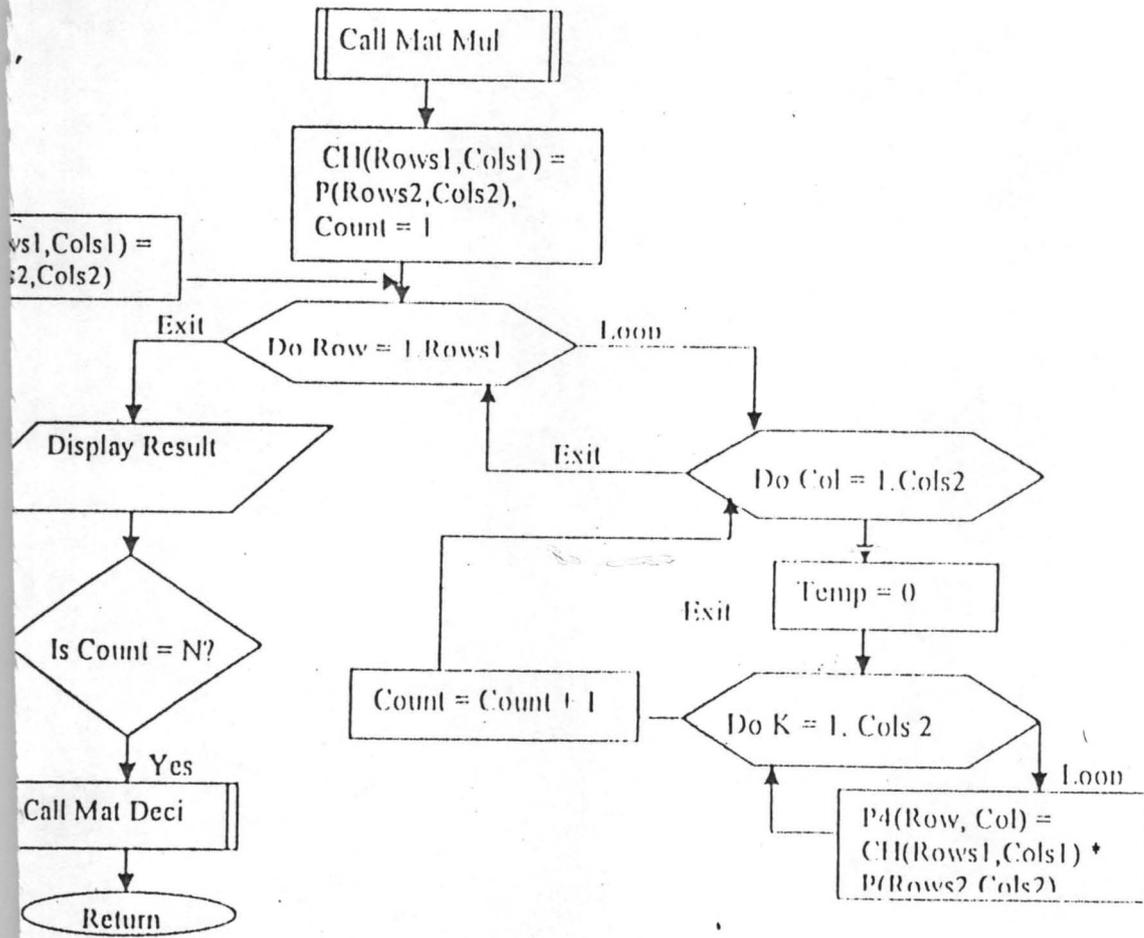
Flow chart for sub procedure addition



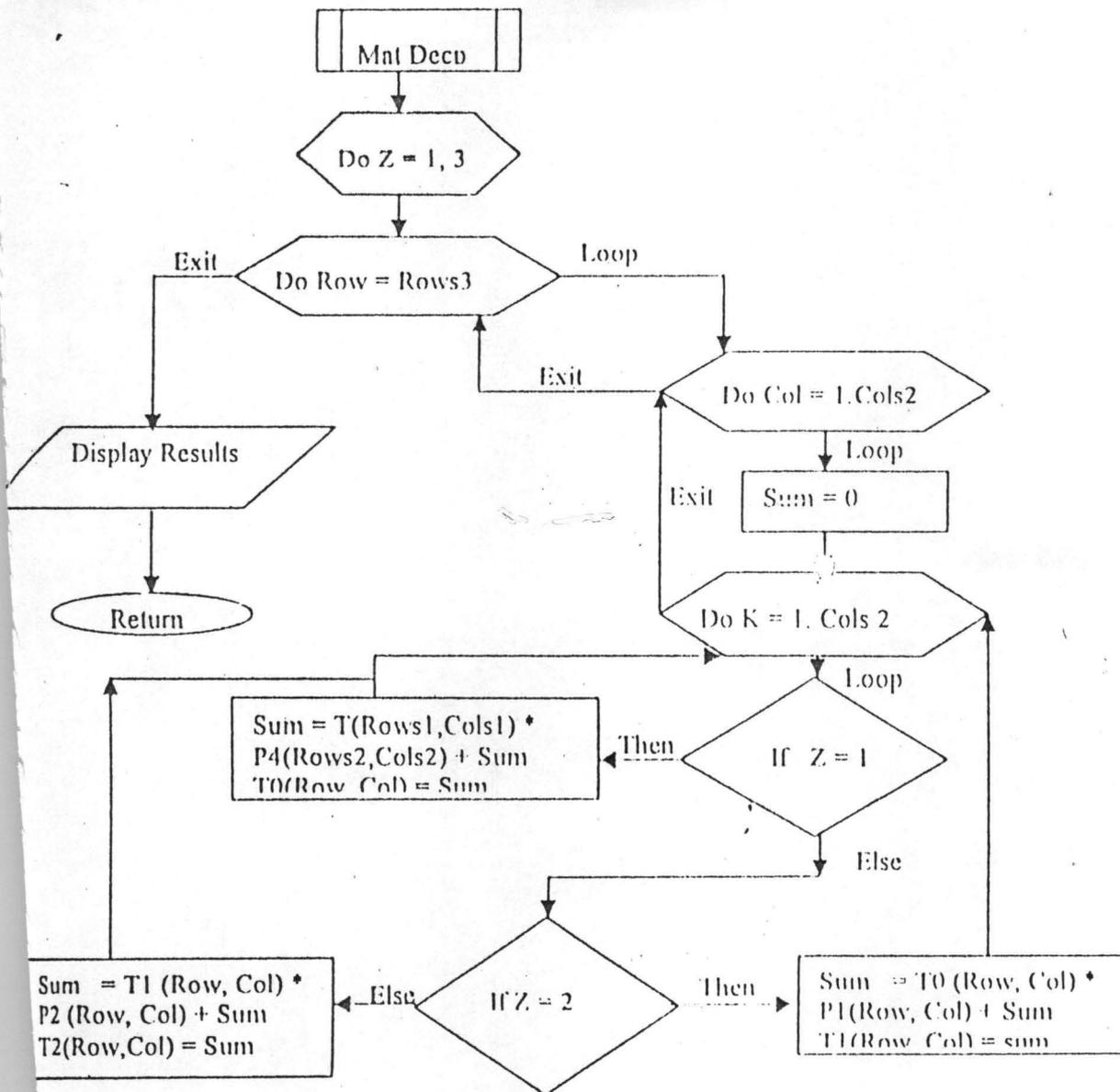
Flow chart for sub procedure product of P1 and P2



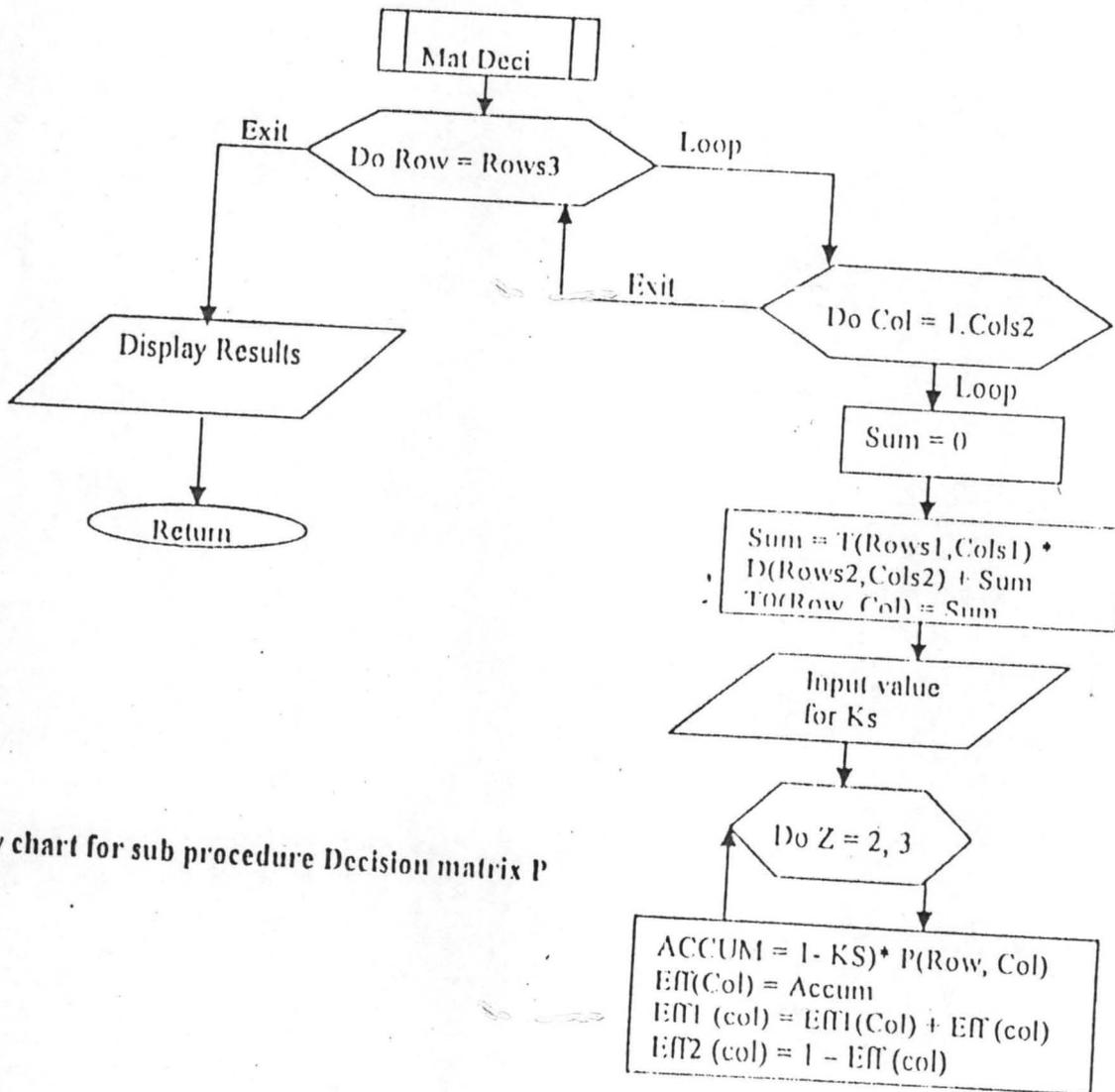
Flow chart for sub procedure iterative Multiplication of transition P4



Flow chart for sub procedure iterative multiplication of transition P



Flow chart for sub procedure iterative multiplication of P with T



Flow chart for sub procedure Decision matrix P

```

*****
* THIS PROGRAM CALCULATES THE ADDITION, DIVISION AND MULTIPLICATION OF *
* SQUARE MATRICES AND A VECTOR MATRIX *
* SIZE, LIMIT, : PARAMETER SPECIFYING MAXIMUM DIMENSIONS OF MATRICES *
* ROWS1        : # OF ROWS IN 1-ST MATRIX *
* COLS1        : # OF COLUMNS IN 1 - MATRIX *
* ROWS2        : # OF ROWS IN 2-ST MATRIX *
* COLS2        : # OF COLUMNS IN 2 - MATRIX *
* ROWS3        : # OF ROWS IN 3-ST MATRIX *
* COLS3        : # OF COLUMNS IN 3 - MATRIX *
* I, J, K, ROW, COL: SUBSCRIPT *
* MAT1         : THE FIRST MATRIX *
* MAT2         : THE SECOND MATRIX *
* FORM        : CHARACTER VARIABLE USED TO OUTPUT ADD *
*****

```

```

COMMON CH(10,10)
INTEGER SIZE, ROWS1, COLS1, ROWS2, COLS2, I, J, K, ROW, COL, ROWS3,
+COLS3, N, TRAIL, BIG, Z, BIG1, G, H, U, V
PARAMETER(SIZE=10)
REAL M1(SIZE, SIZE), M2(SIZE, SIZE), M(SIZE, SIZE), A(SIZE, SIZE),
+T(SIZE, SIZE), SUM, DUM, AWE, WEA, CUM, P(SIZE, SIZE), P1(SIZE, SIZE),
+P2(SIZE, SIZE), L(SIZE, SIZE), X(SIZE, SIZE), R(SIZE, SIZE),
+P4(SIZE, SIZE), B(SIZE, SIZE), C(SIZE, SIZE), D(SIZE, SIZE),
+S(SIZE, SIZE), EFF(SIZE), EFF1, EFF2, KS, P3(SIZE, SIZE)
CHARACTER*12 FORM
CHARACTER*15 GORM
CHARACTER*15 FOUND

```

```

LOGICAL MATCH
LOGICAL FOUND
FOUND = 'OMOHSEMOJE'
DATA FORM /'(1X, ##F8.3)'/
DATA GORM /'(1X, ##F8.2)'/
PRINT *, 'ENTER PASSWORD'
READ *, PWORD

```

```

80 IF(FOUND) THEN
PRINT *, 'ENTER THE VALUE FOR N'
READ 2, N
2 FORMAT(I2)
3 PRINT *, 'ENTER RIGH-JUSTIFIED IN TWO SPACE ZONE THE DIMENSION
+ OF'
PRINT *, 'M1:'
READ '(2I2, TL2, A2)', ROWS1, COLS1, GORM(6:7)
PRINT *, 'M2:'
READ '(2I2, TL2, A2)', ROWS2, COLS2, FORM(6:7)
PRINT *, 'T:'
READ '(2I2)', ROWS3, COLS3

IF (ROWS3 .NE. 1) THEN
IF (COLS3 .NE. COLS1) THEN
PRINT *, 'ROWS3 = 1 AND COLS3 = COLS1 OR COLS2'
GO TO 3
END IF
END IF

```

```

* READ IN M1 AND M2 ROWISE
8 PRINT *, 'ENTER THE ELEMENTS OF MATRIX 1 ROWISE'
IF (A(ROW, COL) .NE. 0) THEN

```

```

READ *, ((A(ROW, COL), COL=1, COLS1), ROW=1, ROWS1)
ELSE
PRINT *, 'ZERO IS NOT ACCEPTABLE FOR DIVISION THAT WILL BE
DONE'
GO TO 8
END IF
9 PRINT *, 'ENTER THE ELEMENTS OF MATRIX 2 ROWISE'
IF (B(ROW, COL) .NE. 0) THEN
READ *, ((B(ROW, COL), COL=1, COLS2), ROW=1, ROWS2)
ELSE
PRINT *, 'ZERO IS NOT ACCEPTABLE FOR DIVISION THAT WILL BE
DONE'
GO TO 9
END IF
PRINT *, 'ENTER THE ELEMENTS OF MATRIX T IN ONE ROW'
READ *, ((T(ROW, COL), COL=1, COLS3), ROW=1, ROWS3)

* PROGRAM TO ADD MATRIX
CALL MATADD(A, B, H, SIZE, ROWS1, COLS1, ROWS2, COLS2, MATCH)
IF (MATCH) THEN
READ (*, *) MMX
PRINT *, 'SUM OF MATRICES H1 AND H2 '
PRINT *, 'H:'
DO 10 ROW = 1, ROWS1
PRINT FORM, (H(ROW, COL), COL=1, COLS2)
10 CONTINUE
END IF

* PROGRAM TO CALCULATE PROBABILITY
CALL MATPRO(CUM, DUM, SUM, ROWS1, ROWS2, SIZE,
+M, A, B, COLS1, COLS2, P1, P2, P, PROD)
READ (*, *) MMX
PRINT *, 'MATRIX PROBABILITY'
PRINT *, 'P1:'
DO 20 ROW = 1, ROWS1
PRINT FORM, (P1(ROW, COL), COL=1, COLS2)
20 CONTINUE
PRINT *, 'P2:'
DO 22 ROW = 1, ROWS1
PRINT FORM, (P2(ROW, COL), COL = 1, COLS2)
22 CONTINUE
PRINT *, 'P:'
DO 28 ROW = 1, ROWS1
PRINT FORM, (P(ROW, COL), COL = 1, COLS2)
28 CONTINUE
READ (*, *) MMX
PRINT *, 'PRODUCT OF MATRICES PROBABILITY'
PRINT *, PROD

* PROGRAM TO CALCULATE PRODUCT OF THE PROBABILITY MATRICES
CALL
MATMUL(P1, P2, P, P, P4, N, ROWS1, ROWS2, COLS1, COLS2, SIZE, ROW, COL,
+T, ROWS3, COLS3, C, R, S, EFF)

READ (*, *) MMX
PRINT *, 'MATRICES P1 AND P2'
PRINT *, 'P1'
DO 37 ROW = 1, ROWS1
PRINT FORM, (P1(ROW, COL), COL = 1, COLS2)
37 CONTINUE
PRINT *, 'P2'

```

```

DO 47 ROW = 1, ROWS1

PRINT FORM, (P2(ROW, COL), COL=1, COLS2)
47 CONTINUE

* PROGRAM TO CALCULATE PRODUCT OF MATRICES P1 AND P2
CALL MATPRD(P1, P2, P, N, ROWS1, COLS1, ROWS2, COLS2, ROWS3, COLS3,
+ SIZE, P4, T, D, L, X)
ELSE
TRAIL = TRAIL + 1
IF (TRAIL .LT. 3) THEN
GO TO 80
ELSE
PRINT *, 'UNAUTHORISE USER STAY CLEAR, BEY FOR NOW'
END IF
END IF
END

*****
*
* THIS SUB PROGRAM IS USED FOR MULTPLICATION OF MATRIXES T AND P4
*
*
*****

* SUBROUTINE DECI(P4, T, D, P, EFF, LIMIT, ROWS3, COLS3, COLS1)
INTEGER ROWS3, COLS3, COLS1, ROW, COL
REAL T(LIMIT, LIMIT), P4(LIMIT, LIMIT), D(LIMIT, LIMIT),
+ P(LIMIT, LIMIT), KS, EFF(LIMIT)
SUM = 0
EFF1 = 0.0
ACCUM = 0.0

DO 21 ROW = 1, ROWS3
DO 14 COL = 1, COLS3
DO 7 K = 1, COLS1
SUM = SUM + T(ROW, K) * P4(K, COL)

7 CONTINUE
D(ROW, COL) = SUM
SUM = 0
14 CONTINUE
21 CONTINUE
PRINT *
PRINT *, 'PREDICTION 1'
DO 108 ROW = 1, 1
PRINT 13, (D(ROW, COL), COL = 1, COLS3)
13 FORMAT(1X, 20(F5.2, 3X))
108 CONTINUE

PRINT *, 'ENTER 0, 0.5, 0.9, 0.99 FOR THE VALUE OF KS'
DO 17 Z = 1, 4
PRINT *, 'ENTER VALUE FOR KS'
READ *, KS
DO 16 ROW = 1, 1
DO 15 COL = 2, COLS3
ACCUM = (1.0 - KS) * P(ROW, COL)
EFF(COL) = ACCUM
EFF1 = EFF1 + ACCUM
PRINT 41, EFF(COL)
15 CONTINUE

```

```

41     FORMAT(2X,F4.2)
16     CONTINUE
      EFF2 = 1.0 - EFF1
      EFF1 = 0
      PRINT 41, EFF2
17     CONTINUE
      RETURN

      END

```

```

*****
*
* THIS SUB PROGRAM IS USED FOR MULTIPLICATION T AND P4, T1 AND TO
*
* T1 AND T2
*
*****
*

```

```

SUBROUTINE DECP(P1,P2,P4,T,D,L,X,LIMIT,ROWS3,COLS3,COLS1)
INTEGER ROWS3,COLS3,COLS1,ROW,COL,K,W,R
REAL T(LIMIT,LIMIT),P4(LIMIT,LIMIT),D(LIMIT,LIMIT),
+L(LIMIT,LIMIT),X(LIMIT,LIMIT),P1(LIMIT,LIMIT),
+P2(LIMIT,LIMIT),SUM,AWE,WEA

```

```

      AWE = 0
      WEA = 0
      SUM = 0
      DO 21 ROW = 1, ROWS3
      DO 14 COL = 1, COLS3
      DO 7 K = 1, COLS1
      SUM = SUM + T(ROW,K) * P4(K,COL)
7      CONTINUE
      D(ROW,COL) = SUM
      SUM = 0
14     CONTINUE
21     CONTINUE

```

```

      READ (*,*) MMX
      PRINT *, 'TO'
      DO 101 ROW = 1, ROWS3
      PRINT 11, (D(ROW,COL), COL = 1, COLS3)
101    CONTINUE

```

```

      DO 42 ROW = 1, 1
      DO 41 COL = 1, COLS3
      DO 17 W = 1, COLS1
      AWE = AWE + D(ROW,W) * P1(W,COL)
17     CONTINUE
      L(ROW,COL) = AWE
      AWE = 0
41     CONTINUE
42     CONTINUE

```

```

      READ(*,*) MMX
      PRINT *, 'T1'
      DO 102 ROW = 1,1
      PRINT 11, (L(ROW,COL), COL = 1, COLS3)
102    CONTINUE

```

```

      DO 49 ROW = 1, 1
      DO 43 COL = 1, COLS3

```

```

DO 87 R = 1, COLS1
WEA = WEA + L(R,ROW,R) * P2(R,COL)
87 CONTINUE
X(ROW,COL) = WEA
WEA = 0
43 CONTINUE
49 CONTINUE

READ(*,*) MMX
PRINT *, 'T2'
DO 103 ROW = 1,1
PRINT 11, (X(ROW,COL), COL = 1, COLS3)
103 CONTINUE

11 FORMAT(1X,20(F4.2,3X))

RETURN
END

```

THIS SUB PROGRAM IS USED FOR ADDITION OF MATRIXES MAT1 AND MAT2

```

SUBROUTINE MATADD(M1,M2,N,LIMIT,ROWS1,COLS1,ROWS2,COLS2,MATCH)
INTEGER ROWS1,COLS1,ROWS2,COLS2,LIMIT,I,J,K,ROW,COL
REAL M1(LIMIT,LIMIT), M2(LIMIT,LIMIT), M(LIMIT,LIMIT)

LOGICAL MATCH
IF (ROWS1 .EQ. ROWS2) THEN
IF (COLS1 .EQ. COLS2) THEN
MATCH = .TRUE.

DO 30 ROW = 1,ROWS1
DO 20 COL = 1,COLS2
M(ROW,COL) = M1(ROW,COL) + M2(ROW,COL)
20 CONTINUE
30 CONTINUE

ELSE
MATCH = .FALSE.
END IF
END IF
RETURN
END

```

THIS SUB PROGRAM IS USED FOR SELF MULTIPLICATION OF MATRIX P

```

SUBROUTINE MATMUL(P1,P2,P,C,P4,N,ROWS1,COLS1,ROWS2,COLS2,LIMIT,
+ROW,COL,T,ROWS3,COLS3,D,L,X,EFF)
COMMON CH(10,10)
INTEGER ROW,COL,K,COUNT,N,ROWS1,ROWS2,COLS1,COLS2,LIMIT,ROWS3,
+COLS3,Q,BIG
REAL P(LIMIT,LIMIT), P4(LIMIT,LIMIT), C(LIMIT,LIMIT),TEMP,

```

```
+T (LIMIT, LIMIT) , D (LIMIT, LIMIT) , P1 (LIMIT, LIMIT) , P2 (LIMIT, LIMIT) ,  
+L (LIMIT, LIMIT) , X (LIMIT, LIMIT) , EFF (LIMIT)
```

```
DO 191 ROW = 1, ROWS1  
DO 191 COL = 1, COLS2  
CH (ROW, COL) = C (ROW, COL)  
191 CONTINUE
```

```
COUNT = 1  
Q = 2  
5 DO 150 ROW = 1, ROWS1  
DO 140 COL = 1, COLS2  
TEMP = 0  
DO 130 K = 1, COLS1  
TEMP = TEMP + CH (ROW, K) * P (K, COL)  
130 CONTINUE  
P4 (ROW, COL) = TEMP  
140 CONTINUE  
150 CONTINUE
```

```
DO 151 ROW = 1, ROWS1  
DO 151 COL = 1, COLS2  
CH (ROW, COL) = P4 (ROW, COL)  
151 CONTINUE
```

```
READ (*, *) MMM  
COUNT = COUNT + 1  
IF (Q .EQ. COUNT) THEN  
PRINT *, 'P(', Q, ')'  
DO 57 ROW = 1, ROWS1  
PRINT 99, (P4 (ROW, COL), COL = 1, COLS1)  
99 FORMAT ( 1X, 80 (F5.3, 3X))  
57 CONTINUE  
Q = Q + 2  
ENDIF  
IF (COUNT .LT. N) THEN  
GO TO 5  
END IF  
CALL DECI (P4, T, D, P, EFF, LIMIT, ROWS3, COLS3, COLS1)  
RETURN  
END
```

THIS SUB PROGRAM IS USED FOR SELF MULTIPLICATION OF MATRIC P3

P3 IS THE PRODUCT OF P1 AND P2

```
SUBROUTINE MATMUT (P1, P2, P3, C, P4, H, ROWS1, COLS1, ROWS2, COLS2, LIMIT,  
+ROW, COL, T, ROWS3, COLS3, D, L, X)  
COMMON CH (10, 10)  
COMMON CH  
INTEGER ROW, COL, K, COUNT, H, ROWS1, ROWS2, COLS1, COLS2, LIMIT, ROWS3,  
+COLS3, Q, BIG  
REAL P3 (LIMIT, LIMIT), P4 (LIMIT, LIMIT), C (LIMIT, LIMIT), TEMP,  
+T (LIMIT, LIMIT), D (LIMIT, LIMIT), P1 (LIMIT, LIMIT), P2 (LIMIT, LIMIT),  
+L (LIMIT, LIMIT), X (LIMIT, LIMIT)
```

```
DO 192 ROW = 1, ROWS1
```

```

DO 192 COL = 1, COLS2
CH(ROW, COL) = C(ROW, COL)
192 CONTINUE
READ(*, *) MMX
COUNT = 1
Q = 2
6 DO 152 ROW = 1, ROWS1
DO 141 COL = 1, COLS2
TEMP = 0
DO 131 K = 1, COLS1
TEMP = TEMP + CH(ROW, K) * P3(K, COL)
131 CONTINUE
P4(ROW, COL) = TEMP
141 CONTINUE
152 CONTINUE

DO 153 ROW = 1, ROWS1
DO 153 COL = 1, COLS2
CH(ROW, COL) = P4(ROW, COL)
153 CONTINUE

READ(*, *) MMM
COUNT = COUNT + 1
IF (Q .EQ. COUNT) THEN
PRINT *, 'P(', Q, ')'
DO 50 ROW = 1, ROWS1
PRINT 109, (P4(ROW, COL), COL = 1, COLS1)
109 FORMAT( 1X, 80(F5.3, 3X))
50 CONTINUE
Q = Q + 2
ENDIF

C(ROW, COL) = TEMP

IF (COUNT .LT. 10) THEN
GO TO 6
END IF
CALL DECP(P1, P2, P4, T, D, L, X, LIMIT, ROWS3, COLS3, COLS1)
RETURN
END

```

.....

THIS SUB PROGRAM IS USED FOR MULTPLICATION OF MATRICES P1 AND P2

.....

```

SUBROUTINE
MATPRD(P1, P2, P3, N, ROWS1, COLS1, ROWS2, COLS2, ROWS3, COLS3,
+LIMIT, P4, T, D, L, X)
INTEGER ROWS1, ROWS2, COLS1, COLS2, SIZE, K, ROW, COL, ROWS3, COLS3
REAL P3(LIMIT, LIMIT), SUM, P1(LIMIT, LIMIT), P2(LIMIT, LIMIT),
+P4(LIMIT, LIMIT), T(LIMIT, LIMIT), D(LIMIT, LIMIT), X(LIMIT, LIMIT),
+L(LIMIT, LIMIT)
BIG = 0
DO 10 ROW = 1, ROWS1
DO 20 COL = 1, COLS2
SUM = 0
DO 30 K = 1, COLS1

```

```

DO 192 COL = 1, COLS2
CH(ROW, COL) = C(ROW, COL)
192 CONTINUE
READ(*, *) MMX
COUNT = 1
Q = 2
6 DO 152 ROW = 1, ROWS1
DO 141 COL = 1, COLS2
TEMP = 0
DO 131 K = 1, COLS1
TEMP = TEMP + CH(ROW, K) * P3(K, COL)
131 CONTINUE
P4(ROW, COL) = TEMP
141 CONTINUE
152 CONTINUE

```

```

DO 153 ROW = 1, ROWS1
DO 153 COL = 1, COLS2
CH(ROW, COL) = P4(ROW, COL)
153 CONTINUE

```

```

READ(*, *) MMM
COUNT = COUNT + 1
IF (Q .EQ. COUNT) THEN
PRINT *, 'P(', Q, ')'
DO 50 ROW = 1, ROWS1
PRINT 109, (P4(ROW, COL), COL = 1, COLS1)
109 FORMAT( 1X, 80(F5.3, 3X))
50 CONTINUE
Q = Q + 2
ENDIF

```

```

C C(ROW, COL) = TEMP

IF (COUNT .LT. 10) THEN
GO TO 6
END IF
CALL DECP(P1, P2, P4, T, D, L, X, LIMIT, ROWS3, COLS3, COLS1)
RETURN
END

```

```

*****
*
* THIS SUB PROGRAM IS USED FOR MULTPLICATION OF MATRIXES P1 AND P2
*
*****
*

```

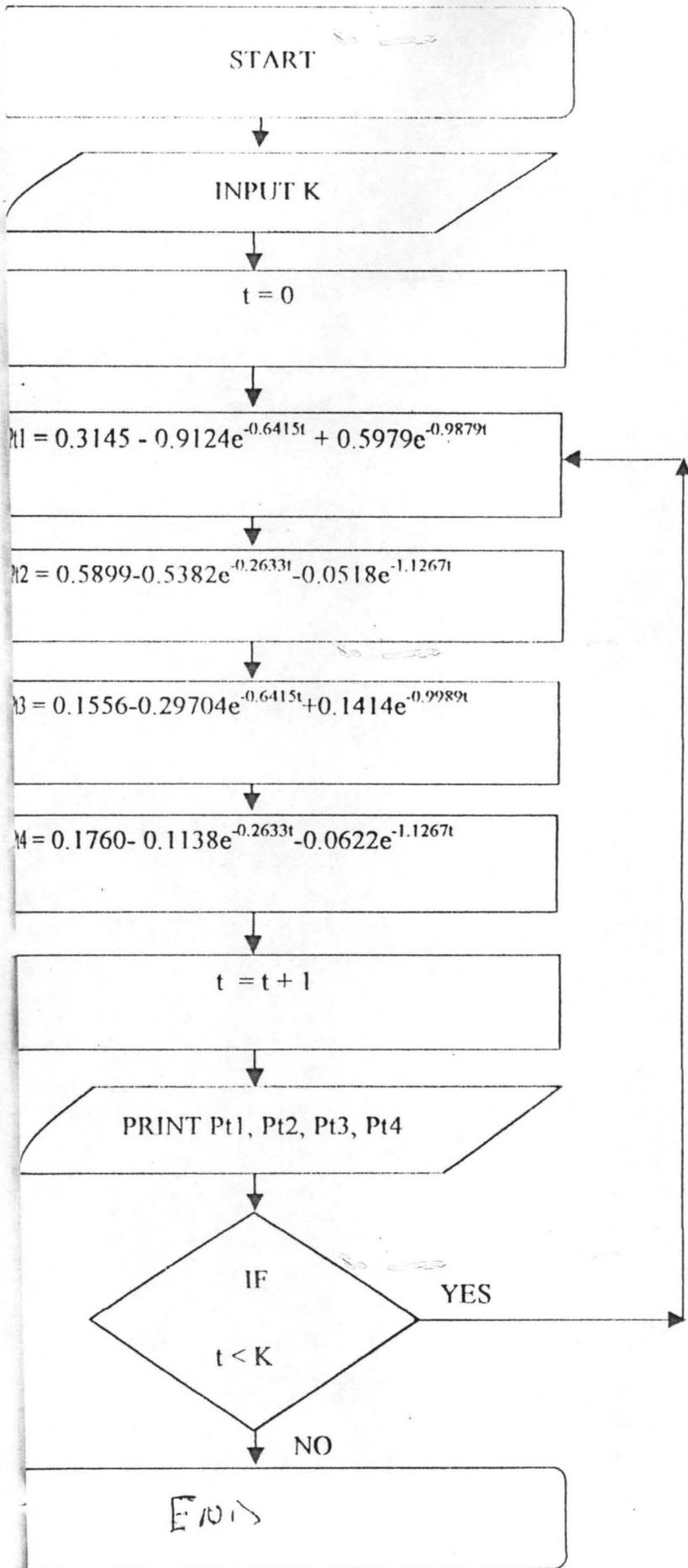
```

SUBROUTINE
MATPRD(P1, P2, P3, N, ROWS1, COLS1, ROWS2, COLS2, ROWS3, COLS3,
+LIMIT, P4, T, D, L, X)
INTEGER ROWS1, ROWS2, COLS1, COLS2, SIZE, K, ROW, COL, ROWS3, COLS3
REAL P3(LIMIT, LIMIT), SUM, P1(LIMIT, LIMIT), P2(LIMIT, LIMIT),
+P4(LIMIT, LIMIT), T(LIMIT, LIMIT), D(LIMIT, LIMIT), X(LIMIT, LIMIT),
+L(LIMIT, LIMIT)
BIG = 0
DO 10 ROW = 1, ROWS1
DO 20 COL = 1, COLS2
SUM = 0
DO 30 K = 1, COLS1

```

APPENDIX B

The following is the algorithm presented in the flowcharts, and the computer programs in the VISUAL BASIC and the output of the program for the Markov chain (discrete state and continuous time) for Catarrh disease.



```
Dim dblPt1 As Double, dblPt2 As Double
Dim dblPt3 As Double, dblPt4 As Double
```

```
ate Sub cmdS_Click()
Rtb.SelText = vbTab & vbTab & "P12(t)" & vbTab & vbTab & vbTab & "P12(t)" & vbTab & vbTab &
vb & vbCrLf
Rtb.SelText = String(60, " ") & vbCrLf
Rtb.SelText = vbTab & "t" & vbTab & vbTab & "K = 0" & vbTab & vbTab & vbTab & "K = 0.99" &
vb & vbTab & vbTab & vbCrLf
Rtb.SelText = String(60, " ") & vbCrLf
For t = 0 To Val(txtA.Text)
dblPt1 = Round(0.3145 - 0.9124 * Exp(-0.6415 * t) + 0.5979 * Exp(-0.9879 * t), 8)
dblPt2 = Abs(Round(0.5899 - 0.5382 * Exp(-0.2633 * t) - 0.0518 * Exp(-1.1267 * t), 8))
Rtb.SelText = vbTab & t & vbTab & vbTab & dblPt1 & vbTab & vbTab & vbTab & dblPt2 & vbTab &
vb & vbTab & vbCrLf
Next t
Rtb.SelText = vbCrLf & vbCrLf
```

```
Rtb.SelText = vbTab & vbTab & "P13(t)" & vbTab & vbTab & vbTab & "P13(t)" & vbTab & vbTab &
vb & vbCrLf
Rtb.SelText = String(60, " ") & vbCrLf
Rtb.SelText = vbTab & "t" & vbTab & vbTab & "K = 0" & vbTab & vbTab & vbTab & "K = 0.99" &
vbTab & vbTab & vbTab & vbCrLf
Rtb.SelText = String(60, " ") & vbCrLf
For t = 0 To Val(txtA.Text)
dblPt3 = Abs(Round(0.1556 - 0.29704 * Exp(-0.6415 * t) + 0.1414 * Exp(-0.9989 * t), 8))
dblPt4 = Round(0.176 - 0.1138 * Exp(-0.2633 * t) - 0.0622 * Exp(-1.1267 * t), 8)
Rtb.SelText = vbTab & t & vbTab & vbTab & dblPt3 & vbTab & vbTab & vbTab & dblPt4 & vbTab &
vbTab & vbTab & vbCrLf
Next t
Sub
```

```
ate Sub Form_MouseUp(Button As Integer, Shift As Integer, X As Single, Y As Single)
If Button = vbRightButton Then
ABU.PopupMenu mnufile
End If
Sub
```

```
ate Sub mnuexit_Click()
End
Sub
```

```
ate Sub mnuprint_Click()
On Error Resume Next
If ABU Is Nothing Then Exit Sub
```

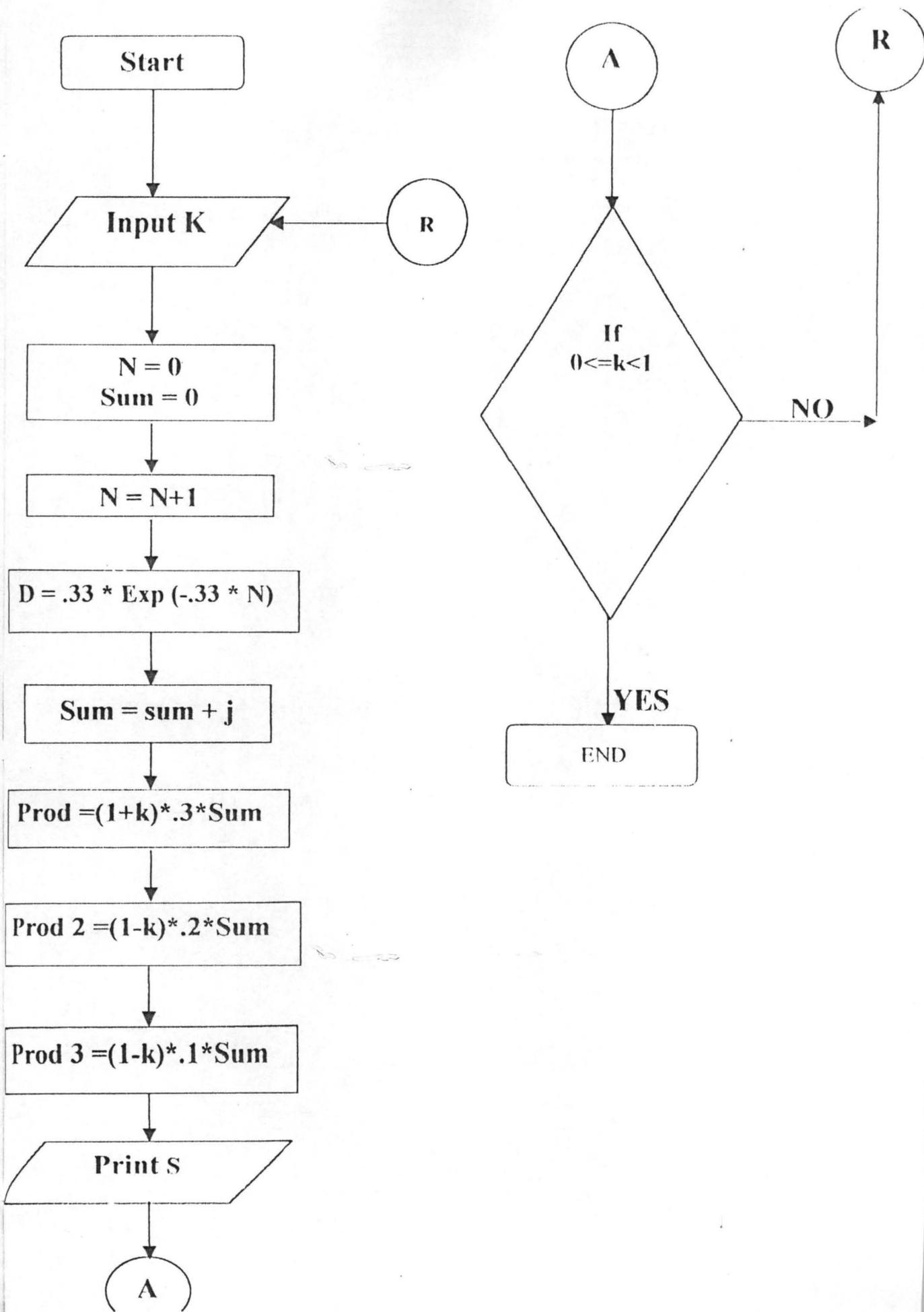
```
With CommonDialog1
.DialogTitle = "Print"
.CancelError = True
.Flags = cdlPDReturnDC + cdlPDNoPageNums
If Rtb.SelLength = 0 Then
.Flags = .Flags + cdlPDAllPages
Else
.Flags = .Flags + cdlPDSelection
End If
.ShowPrinter
If Err <> MSError.cdlCancel Then
Rtb.SelPrint .hDC
End If
End With
Sub
```

| P12(t) | | P12(t) | |
|--------|------------|------------|------------|
| t | K = 0 | K = 0.99 | |
| 0 | 0 | 0.0001 | |
| 1 | 0.05675225 | | 0.15949878 |
| 2 | 0.14447771 | | 0.26659275 |
| 3 | 0.2122045 | | 0.34385282 |
| 4 | 0.25588307 | | 0.40159367 |
| 5 | 0.28186633 | | 0.44543846 |
| 6 | 0.29665859 | | 0.47896199 |
| 7 | 0.30486081 | | 0.50466957 |
| 8 | 0.30933348 | | 0.5244081 |
| 9 | 0.31174575 | | 0.53957153 |
| 10 | 0.3130372 | | 0.55122291 |
| 11 | 0.31372511 | | 0.56017652 |
| 12 | 0.31409026 | | 0.56705726 |
| 13 | 0.31428362 | | 0.57234513 |
| 14 | 0.31438583 | | 0.57640889 |
| 15 | 0.3144398 | | 0.57953193 |
| 16 | 0.31446827 | | 0.58193203 |
| 17 | 0.31448328 | | 0.58377652 |
| 18 | 0.31449119 | | 0.58519404 |
| 19 | 0.31449536 | | 0.58628341 |
| 20 | 0.31449756 | | 0.58712061 |
| 21 | 0.31449871 | | 0.58776401 |
| 22 | 0.31449932 | | 0.58825847 |
| 23 | 0.31449964 | | 0.58863846 |
| 24 | 0.31449981 | | 0.5889305 |
| 25 | 0.3144999 | | 0.58915492 |
| 26 | 0.31449995 | | 0.5893274 |
| 27 | 0.31449997 | | 0.58945995 |
| 28 | 0.31449999 | | 0.58956182 |
| 29 | 0.31449999 | | 0.5896401 |
| 30 | 0.3145 | 0.58970027 | |
| 31 | 0.3145 | 0.5897465 | |
| 32 | 0.3145 | 0.58978204 | |
| 33 | 0.3145 | 0.58980934 | |
| 34 | 0.3145 | 0.58983033 | |
| 35 | 0.3145 | 0.58984646 | |
| 36 | 0.3145 | 0.58985885 | |
| 37 | 0.3145 | 0.58986838 | |
| 38 | 0.3145 | 0.5898757 | |
| 39 | 0.3145 | 0.58988132 | |
| 40 | 0.3145 | 0.58988565 | |
| 41 | 0.3145 | 0.58988877 | |
| 42 | 0.3145 | 0.58989152 | |
| 43 | 0.3145 | 0.58989349 | |
| 44 | 0.3145 | 0.58989499 | |
| 45 | 0.3145 | 0.58989615 | |
| 46 | 0.3145 | 0.58989704 | |
| 47 | 0.3145 | 0.58989773 | |
| 48 | 0.3145 | 0.58989825 | |
| 49 | 0.3145 | 0.58989866 | |
| 50 | 0.3145 | 0.58989897 | |

| P13(t) | | P13(t) | |
|--------|------------|--------|------------|
| t | K = 0 | | K = 0.99 |
| 0 | 0.00004 | | 0 |
| 1 | 0.05128323 | | 0.06838433 |
| 2 | 0.09243775 | | 0.10225504 |
| 3 | 0.11931056 | | 0.12222976 |
| 4 | 0.13537601 | | 0.13561802 |
| 5 | 0.14454047 | | 0.14527099 |
| 6 | 0.14962556 | | 0.15248326 |
| 7 | 0.15239862 | | 0.15795915 |
| 8 | 0.15389391 | | 0.16214579 |
| 9 | 0.15469417 | | 0.16535625 |
| 10 | 0.15512029 | | 0.16782125 |
| 11 | 0.1553464 | | 0.16971489 |
| 12 | 0.1554661 | | 0.17116994 |
| 13 | 0.15552936 | | 0.17228808 |
| 14 | 0.15556276 | | 0.17314736 |
| 15 | 0.15558037 | | 0.17380772 |
| 16 | 0.15558966 | | 0.17431521 |
| 17 | 0.15559455 | | 0.17470522 |
| 18 | 0.15559713 | | 0.17500495 |
| 19 | 0.15559849 | | 0.17523529 |
| 20 | 0.1555992 | | 0.17541231 |
| 21 | 0.15559958 | | 0.17554835 |
| 22 | 0.15559978 | | 0.17565291 |
| 23 | 0.15559988 | | 0.17573325 |
| 24 | 0.15559994 | | 0.175795 |
| 25 | 0.15559997 | | 0.17584246 |
| 26 | 0.15559998 | | 0.17587893 |
| 27 | 0.15559999 | | 0.17590695 |
| 28 | 0.1556 | | 0.17592849 |
| 29 | 0.1556 | | 0.17594505 |
| 30 | 0.1556 | | 0.17595777 |
| 31 | 0.1556 | | 0.17596754 |
| 32 | 0.1556 | | 0.17597506 |
| 33 | 0.1556 | | 0.17598083 |
| 34 | 0.1556 | | 0.17598527 |
| 35 | 0.1556 | | 0.17598868 |
| 36 | 0.1556 | | 0.1759913 |
| 37 | 0.1556 | | 0.17599331 |
| 38 | 0.1556 | | 0.17599486 |
| 39 | 0.1556 | | 0.17599605 |
| 40 | 0.1556 | | 0.17599697 |
| 41 | 0.1556 | | 0.17599767 |
| 42 | 0.1556 | | 0.17599821 |
| 43 | 0.1556 | | 0.17599862 |
| 44 | 0.1556 | | 0.17599894 |
| 45 | 0.1556 | | 0.17599919 |
| 46 | 0.1556 | | 0.17599937 |
| 47 | 0.1556 | | 0.17599952 |
| 48 | 0.1556 | | 0.17599963 |
| 49 | 0.1556 | | 0.17599972 |
| 50 | 0.1556 | | 0.17599978 |

APPENDIX C

The following is the algorithm presented in the flowcharts, and the computer programs in QBASIC and the program output for the Semi - Markov model *for* Leprosy disease.



```

= 0
WT "ENTER THE RANGE OF VALUES "; N
WT "NUMBER", "EXPONENT SUM"; SPC(7); "EXPONENT SUM *.3"
WT "-----", "-----"; SPC(7); "-----"
k = 1 TO N
.33 * EXP(-.33 * k)
= sum + j
i = .3 * sum
WT k, USING ("#.#####"); sum; SPC(8); prod
k = 20 OR k = 41 OR k = 62 OR k = 83 THEN PRINT "press any key to continue"
k

```

```

sum = 0
INPUT "ENTER THE RANGE OF VALUES "; N
INPUT "enter the value of k:", k: CLS : PRINT
LOCATE 1, 20: PRINT "FOR VALUE OF K="; k
PRINT SPC(10); "@12", SPC(12); "@13"; SPC(10); "@14":
FOR s = 1 TO N
    j = (.152380952# * (s / 10.5) ^ .6) * (EXP(-(s / 10.5)) ^ 1.6)
    Sum = Sum + j
    prod = (1 + k) * .3 * Sum
    prod2 = (1 - k) * .2 * Sum
    prod3 = (1 - k) * .1 * Sum
PRINT s; USING ("#.#####"); SPC(4); prod; SPC(4); prod2; SPC(4); prod3
IF s = 20 OR s = 43 OR s = 66 OR s = 89 THEN PRINT "PRESS ANY KEY TO CONTINUE";
PRINT s

```

m = 0

```
INPUT "ENTER THE RANGE OF VALUES "; N
INPUT "enter the value of k:", K: CLS : PRINT
PRINT "FOR K="; K
PRINT "s"; SPC(12); "@12", SPC(12); "@13"; SPC(10); "@14": PRINT
  FOR s = 1 TO N
    j = 1 - EXP(-.33 * s)
    prod = (1 + K) * .3 * j
    prod2 = (1 - K) * .2 * j
    prod3 = (1 - K) * .1 * j
    PRINT s; USING ("#.#####"); SPC(10); prod; SPC(10); prod2; SPC(4); p
  'IF s = 21 OR s = 44 OR s = 66 THEN PRINT "press any key to continue:"; INP
  RT s
```

m = 0

```
INPUT "ENTER THE RANGE OF VALUES "; N
INPUT "enter the value of k:", k: CLS
LOCATE 1, 25: PRINT " FOR K= "; k
PRINT SPC(5); SPC(10); "@12", SPC(12); "@13"; SPC(10); "@14": PRINT
FOR s = 1 TO N
    j = (1 - EXP(-(s / 10.5)) ^ 1.6)
    prod = (1 + k) * .3 * j
    prod2 = (1 - k) * .2 * j
    prod3 = (1 - k) * .1 * j
PRINT s; USING ("#.#####"); SPC(10); prod; SPC(10); prod2; SPC(4); prod3
= 20 OR s = 43 OR s = 65 OR s = 87 THEN PRINT "press any key to continue:"
PRINT s
```

THE RESULT OF DISCRETE STATE AND DISCRETE TIME FOR
EXPONENTIAL STARTS FROM THE NEXT PAGE

| | | | |
|----|--------------|--------------|---------------|
| 1 | 0.0237744044 | 0.0211734503 | 0.0737440704 |
| 2 | 0.4078005004 | 0.1222417746 | 0.0015611631 |
| 3 | 0.5304270850 | 0.1501270315 | 0.1050852105 |
| 4 | 0.6105007506 | 0.1055742335 | 0.1227161532 |
| 5 | 0.6018777470 | 0.2045071764 | 0.1363914460 |
| 6 | 0.7275010002 | 0.2102560414 | 0.145040276 |
| 7 | 0.750763176 | 0.2200201102 | 0.1520555635 |
| 8 | 0.702255167 | 0.235147609 | 0.1567651033 |
| 9 | 0.6007555200 | 0.240267000 | 0.1601511740 |
| 10 | 0.0172231005 | 0.2420701261 | 0.162054224 |
| 11 | 0.015773060 | 0.245022100 | 0.1647375774 |
| 12 | 0.0170602000 | 0.249004009 | 0.165936300 |
| 13 | 0.017000614 | 0.2477772614 | 0.1664001603 |
| 14 | 0.0377472040 | 0.2507227063 | 0.1671404560 |
| 15 | 0.030700101 | 0.2514230550 | 0.1676150650 |
| 16 | 0.037600205 | 0.251200010 | 0.1679520607 |
| 17 | 0.040604300 | 0.2520005460 | 0.1681076030 |
| 18 | 0.041030000 | 0.252511006 | 0.1683674000 |
| 19 | 0.0426547072 | 0.2527304460 | 0.168424437 |
| 20 | 0.0427010217 | 0.2520731227 | 0.1685020660 |
| 21 | 0.0472231005 | 0.252600060 | 0.1686656107 |
| 22 | 0.0476551717 | 0.2530305607 | 0.1686030360 |
| 23 | 0.047000000 | 0.2530000000 | 0.1687262005 |
| 24 | 0.047010073 | 0.2531255702 | 0.1687503004 |
| 25 | 0.043000000 | 0.2531514460 | 0.1687676162 |
| 26 | 0.030000000 | 0.2531700432 | 0.1687800130 |
| 27 | 0.0307440000 | 0.2531803745 | 0.1687800007 |
| 28 | 0.030766665 | 0.2531020200 | 0.1687053223 |
| 29 | 0.030000000 | 0.2531000052 | 0.1687000360 |
| 30 | 0.0401625230 | 0.2532040021 | 0.168802057 |
| 31 | 0.040001740 | 0.2532004504 | 0.1688056130 |
| 32 | 0.040067570 | 0.2532110512 | 0.16880073575 |
| 33 | 0.040400000 | 0.2532120602 | 0.1688005704 |
| 34 | 0.0404730000 | 0.2532142103 | 0.1688004506 |
| 35 | 0.040504670 | 0.2532151630 | 0.16880100004 |
| 36 | 0.040527320 | 0.2532150106 | 0.16880105464 |
| 37 | 0.040544000 | 0.2532162262 | 0.16880100001 |
| 38 | 0.040555030 | 0.2532166030 | 0.1688011275 |
| 39 | 0.040564275 | 0.2532165021 | 0.1688012015 |
| 40 | 0.040570235 | 0.2532171300 | 0.1688014107 |
| 41 | 0.040574400 | 0.2532172501 | 0.1688014062 |
| 42 | 0.040577300 | 0.2532173205 | 0.1688015440 |
| 43 | 0.0405770772 | 0.2532173001 | 0.1688016014 |
| 44 | 0.040581550 | 0.2532174507 | 0.1688016342 |
| 45 | 0.040582752 | 0.2532174005 | 0.1688016640 |
| 46 | 0.040583340 | 0.2532175103 | 0.1688016640 |
| 47 | 0.040583014 | 0.2532175103 | 0.1688016700 |
| 48 | 0.040584570 | 0.2532175401 | 0.1688016930 |
| 49 | 0.040585136 | 0.2532175370 | 0.1688017007 |
| 50 | 0.040585136 | 0.2532175770 | 0.1688017007 |

FOR VALUE OF K = .5

| NUM | 012 | 013 | 014 | |
|-----|--------------|--------------|--------------|--------------|
| 1 | 0.2372418444 | 0.1067601015 | 0.0237241852 | 0.0110622426 |
| 2 | 0.4070000000 | 0.1035126132 | 0.0407005015 | 0.0203002000 |
| 3 | 0.5304200050 | 0.2306017472 | 0.0530426002 | 0.0265213046 |
| 4 | 0.6105007506 | 0.2703613503 | 0.0610500766 | 0.0303200303 |
| 5 | 0.6010572440 | 0.3060007721 | 0.0601057230 | 0.0340070615 |
| 6 | 0.7275201002 | 0.3273040547 | 0.0727520130 | 0.0363760060 |
| 7 | 0.7602761176 | 0.3421243420 | 0.0760276310 | 0.0380130150 |
| 8 | 0.7030251167 | 0.3527214025 | 0.0703025517 | 0.0391012750 |
| 9 | 0.0007556200 | 0.3603400200 | 0.0000755620 | 0.0400377010 |
| 10 | 0.0120170673 | 0.3650173002 | 0.0012027112 | 0.0406463556 |
| 11 | 0.0216773060 | 0.3687540500 | 0.0021677372 | 0.0410030606 |
| 12 | 0.0270602300 | 0.3725057130 | 0.0027060270 | 0.0413004135 |
| 13 | 0.0324010614 | 0.3746200145 | 0.0032440047 | 0.0416245423 |
| 14 | 0.0357422340 | 0.3760040505 | 0.0035742200 | 0.0417071140 |
| 15 | 0.0300700101 | 0.3771350324 | 0.0030070025 | 0.0410030113 |
| 16 | 0.0307613035 | 0.3770021664 | 0.0030760303 | 0.0410000152 |
| 17 | 0.0400604300 | 0.3704350203 | 0.0040060415 | 0.0420404200 |
| 18 | 0.0410210000 | 0.3700260400 | 0.0041027004 | 0.0420010502 |
| 19 | 0.0424614072 | 0.3701076541 | 0.0042461417 | 0.0421230710 |
| 20 | 0.0420103104 | 0.3703006010 | 0.0042010334 | 0.0421455167 |
| 21 | 0.0432131005 | 0.3704544100 | 0.0043233004 | 0.0421616547 |
| 22 | 0.0434651404 | 0.3705503301 | 0.0043465170 | 0.0421732500 |
| 23 | 0.0436310020 | 0.3706344101 | 0.0043631000 | 0.0421015000 |
| 24 | 0.0437510073 | 0.3706003021 | 0.0043751052 | 0.0421075076 |
| 25 | 0.0430300057 | 0.3707271550 | 0.0043030001 | 0.0421010040 |
| 26 | 0.0430000045 | 0.3707550400 | 0.0043000070 | 0.0421050035 |
| 27 | 0.0430446600 | 0.3707751060 | 0.0043044600 | 0.0421072340 |
| 28 | 0.0430766665 | 0.3707005312 | 0.0043076662 | 0.0421000331 |
| 29 | 0.0430006030 | 0.3707000726 | 0.0043000604 | 0.0421000042 |
| 30 | 0.0430162530 | 0.3700073232 | 0.0044016200 | 0.0422000040 |
| 31 | 0.0430201740 | 0.3700126076 | 0.0044020220 | 0.0422014110 |
| 32 | 0.0430367370 | 0.3700165610 | 0.0044036700 | 0.0422010304 |
| 33 | 0.0430420072 | 0.3700103336 | 0.0044042007 | 0.0422021440 |
| 34 | 0.0430473000 | 0.3700213005 | 0.0044047203 | 0.0422023647 |
| 35 | 0.0430504670 | 0.3700227310 | 0.0044050407 | 0.0422025240 |
| 36 | 0.0430527220 | 0.3700237443 | 0.0044052732 | 0.0422026366 |
| 37 | 0.0430544000 | 0.3700244004 | 0.0044054446 | 0.0422027223 |
| 38 | 0.0430555030 | 0.3700250250 | 0.0044055630 | 0.0422027010 |
| 39 | 0.0430564275 | 0.3700254132 | 0.0044056467 | 0.0422020220 |
| 40 | 0.0430570235 | 0.3700256014 | 0.0044057053 | 0.0422020527 |
| 41 | 0.0430574400 | 0.3700250603 | 0.0044057426 | 0.0422020713 |
| 42 | 0.0430577300 | 0.3700260003 | 0.0044057724 | 0.0422020062 |
| 43 | 0.0430570772 | 0.3700260007 | 0.0044050022 | 0.0422020011 |
| 44 | 0.0430501560 | 0.3700261001 | 0.0044050171 | 0.0422020005 |
| 45 | 0.0430502752 | 0.3700262477 | 0.0044050320 | 0.0422020160 |
| 46 | 0.0430503340 | 0.3700262775 | 0.0044050320 | 0.0422020160 |
| 47 | 0.0430503044 | 0.3700263073 | 0.0044050304 | 0.0422020107 |
| 48 | 0.0430504540 | 0.3700263073 | 0.0044050460 | 0.0422020234 |
| 49 | 0.0430505136 | 0.3700263371 | 0.0044050543 | 0.0422020272 |
| 50 | 0.0430505136 | 0.3700263371 | 0.0044050543 | 0.0422020272 |

THE RESULT OF DISCRETE STATE AND DISCRETE TIME FOR WEIBULL
STARTS FROM THE NEXT PAGE

FOR VALUE OF R= 0

| | 012 | 013 | 014 |
|----|--------------|---------------|--------------|
| 1 | 0.0005754713 | 0.00030936472 | 0.0031010236 |
| 2 | 0.0220370200 | 0.0146010000 | 0.0073450405 |
| 3 | 0.0356000533 | 0.0237007022 | 0.0110053511 |
| 4 | 0.0496131015 | 0.0330754510 | 0.0165377250 |
| 5 | 0.0632050000 | 0.0421000500 | 0.0210050300 |
| 6 | 0.0763017355 | 0.0500211533 | 0.0254605766 |
| 7 | 0.0887170350 | 0.0551446050 | 0.0295723435 |
| 8 | 0.1001024053 | 0.0667040310 | 0.0333074650 |
| 9 | 0.1107670043 | 0.0730140320 | 0.0360224650 |
| 10 | 0.1204402004 | 0.0802035207 | 0.0401467644 |
| 11 | 0.1292340504 | 0.0861655620 | 0.0430702010 |
| 12 | 0.1371011010 | 0.0914607272 | 0.0457303636 |
| 13 | 0.1443500330 | 0.0962302037 | 0.0480110640 |
| 14 | 0.1507035077 | 0.1005200076 | 0.0502645030 |
| 15 | 0.1565521657 | 0.1043001055 | 0.0521040520 |
| 16 | 0.1616021127 | 0.1077047303 | 0.0530071367 |
| 17 | 0.1667600030 | 0.1100460575 | 0.0537020200 |
| 18 | 0.1703302763 | 0.1135575175 | 0.0547075000 |
| 19 | 0.1730437500 | 0.1150675053 | 0.0570012527 |
| 20 | 0.1771301705 | 0.1100021107 | 0.0500460500 |
| 21 | 0.1700625000 | 0.1100750520 | 0.050075024 |
| 22 | 0.1624564407 | 0.1216376340 | 0.0600100175 |
| 23 | 0.1646556062 | 0.1231037074 | 0.0615510007 |
| 24 | 0.1665020514 | 0.1243053034 | 0.0611076517 |
| 25 | 0.1600076502 | 0.1255317777 | 0.0627050000 |
| 26 | 0.1607062000 | 0.1265300410 | 0.0632654705 |
| 27 | 0.1611125332 | 0.1274003555 | 0.0637041777 |
| 28 | 0.1622676061 | 0.1281704624 | 0.0640002312 |
| 29 | 0.1632006020 | 0.1280537020 | 0.0644760015 |
| 30 | 0.1641603000 | 0.1284455075 | 0.0647227000 |
| 31 | 0.1640457675 | 0.1280630450 | 0.0640010225 |
| 32 | 0.1656260040 | 0.1304173017 | 0.0652006050 |
| 33 | 0.1662211720 | 0.1300141202 | 0.0654070601 |
| 34 | 0.1667413574 | 0.1311600000 | 0.0655004500 |
| 35 | 0.1671050727 | 0.1314630151 | 0.0657310576 |
| 36 | 0.1675027000 | 0.1317205150 | 0.0650642575 |
| 37 | 0.1670302610 | 0.1310504070 | 0.0650707400 |
| 38 | 0.1602415617 | 0.1321610361 | 0.0660005101 |
| 39 | 0.1605052070 | 0.1323367053 | 0.0661603077 |
| 40 | 0.1607350434 | 0.1324000240 | 0.0662450120 |
| 41 | 0.1600353507 | 0.1326735602 | 0.0663147044 |
| 42 | 0.1601000512 | 0.1327300015 | 0.0663600500 |
| 43 | 0.1602610703 | 0.1320412145 | 0.0664206073 |
| 44 | 0.1603041367 | 0.1320204204 | 0.0664647147 |
| 45 | 0.1605002770 | 0.1330061053 | 0.0665030026 |
| 46 | 0.1606004733 | 0.1330720723 | 0.0665364061 |
| 47 | 0.1606066004 | 0.1331310710 | 0.0665555360 |
| 48 | 0.1607723077 | 0.1331015060 | 0.0665007034 |
| 49 | 0.1600302650 | 0.1332255000 | 0.0666127503 |
| 50 | 0.1600055100 | 0.1332636774 | 0.0666310307 |
| 51 | 0.1600452561 | 0.1332400324 | 0.0666404162 |
| 52 | 0.1600004044 | 0.1333256513 | 0.0666620256 |
| 53 | 0.2000260204 | 0.1333506703 | 0.0666753352 |
| 54 | 0.2000500002 | 0.1333724111 | 0.0666062056 |
| 55 | 0.2000060215 | 0.1333012760 | 0.0666056300 |
| 56 | 0.2001114035 | 0.1334076524 | 0.0667030262 |
| 57 | 0.2001320021 | 0.1334210601 | 0.0667100340 |
| 58 | 0.2001512045 | 0.1334341013 | 0.0667170057 |
| 59 | 0.2001673201 | 0.1334440004 | 0.0667224452 |
| 60 | 0.2001012450 | 0.1334541500 | 0.0667270705 |
| 61 | 0.2001033157 | 0.1334622055 | 0.0667311020 |
| 62 | 0.2002037764 | 0.1334601703 | 0.0667345006 |
| 63 | 0.2002120263 | 0.1334752001 | 0.0667376146 |
| 64 | 0.2002070741 | 0.1334004744 | 0.0667400372 |
| 65 | 0.2002275130 | 0.1334050043 | 0.0667426092 |
| 66 | 0.2002334140 | 0.1334000302 | 0.0667444601 |

FOR VALUE OF K= .5

| | 012 | 013 | 014 |
|----|--------------|---------------|--------------|
| 1 | 0.0143032000 | 0.0031010236 | 0.0015050110 |
| 2 | 0.0330567323 | 0.0073450405 | 0.0036720702 |
| 3 | 0.0535200037 | 0.0110053511 | 0.0059476756 |
| 4 | 0.0744107667 | 0.0165377250 | 0.0082600630 |
| 5 | 0.0940276300 | 0.0210050300 | 0.0105475150 |
| 6 | 0.1145725005 | 0.0254605766 | 0.0127302003 |
| 7 | 0.1330755502 | 0.0295723435 | 0.0147061717 |
| 8 | 0.1502005067 | 0.0333074650 | 0.0166007330 |
| 9 | 0.1661510015 | 0.0350224660 | 0.0184512330 |
| 10 | 0.1806604415 | 0.0401467644 | 0.0200733022 |
| 11 | 0.1938522607 | 0.0430702010 | 0.0215301405 |
| 12 | 0.2057066454 | 0.0457303636 | 0.0228651010 |
| 13 | 0.2165303046 | 0.0481106410 | 0.0240500200 |
| 14 | 0.2261002600 | 0.0502645030 | 0.0251322510 |
| 15 | 0.2340202337 | 0.0521040520 | 0.0260720254 |
| 16 | 0.2405301600 | 0.0538073607 | 0.0269406040 |
| 17 | 0.2450402257 | 0.0554220200 | 0.0277115144 |
| 18 | 0.2485504423 | 0.0568770750 | 0.0283003704 |
| 19 | 0.2500156370 | 0.0570012527 | 0.0288000263 |
| 20 | 0.2557072042 | 0.0580460500 | 0.0295230200 |
| 21 | 0.2600430030 | 0.0590007526 | 0.0299037632 |
| 22 | 0.2736046005 | 0.0600100175 | 0.0304004007 |
| 23 | 0.2750035501 | 0.0615510007 | 0.0307750444 |
| 24 | 0.2700004346 | 0.0621076517 | 0.0310000250 |
| 25 | 0.2074465036 | 0.0627650000 | 0.0313020444 |
| 26 | 0.2046044034 | 0.0632654205 | 0.0316327102 |
| 27 | 0.2066600073 | 0.0637041777 | 0.0318520000 |
| 28 | 0.2004015441 | 0.0640002312 | 0.0320446156 |
| 29 | 0.2000210155 | 0.0644260015 | 0.0322134450 |
| 30 | 0.2012525033 | 0.0647227000 | 0.0323613004 |
| 31 | 0.2024106507 | 0.0640010225 | 0.0324000613 |
| 32 | 0.2034301400 | 0.0652006050 | 0.0326043470 |
| 33 | 0.2043317502 | 0.0654070601 | 0.0327035300 |
| 34 | 0.2051120436 | 0.0655004500 | 0.0327002250 |
| 35 | 0.2057030015 | 0.0657310576 | 0.0328650700 |
| 36 | 0.2063001625 | 0.06580642575 | 0.0329031200 |
| 37 | 0.2060000052 | 0.0650707400 | 0.0320000745 |
| 38 | 0.2073023276 | 0.06600005101 | 0.0330000560 |
| 39 | 0.2077570044 | 0.0661003077 | 0.0330001000 |
| 40 | 0.2001025577 | 0.0662450120 | 0.0331225000 |
| 41 | 0.2004030247 | 0.0663117041 | 0.0331550020 |
| 42 | 0.2006647705 | 0.0663600500 | 0.0331040754 |
| 43 | 0.2000027364 | 0.0664206073 | 0.0332103036 |
| 44 | 0.2000012100 | 0.0664647147 | 0.0332323574 |
| 45 | 0.2002030244 | 0.0665030026 | 0.0332515463 |
| 46 | 0.2004141077 | 0.0665364061 | 0.0332602431 |
| 47 | 0.2005440007 | 0.0665655360 | 0.0332077600 |
| 48 | 0.2006505667 | 0.0665007034 | 0.0332053067 |
| 49 | 0.2007573012 | 0.0666127503 | 0.0333063751 |
| 50 | 0.2000432015 | 0.0666310307 | 0.0333150103 |
| 51 | 0.2000470767 | 0.0666404162 | 0.0333242001 |
| 52 | 0.2000077266 | 0.0666620266 | 0.0333314120 |
| 53 | 0.2000300232 | 0.0666753352 | 0.0333370076 |
| 54 | 0.2000070700 | 0.0666002066 | 0.0333431000 |
| 55 | 0.2001303073 | 0.0666056300 | 0.0333470100 |
| 56 | 0.2001672320 | 0.0667003072 | 0.0333510131 |
| 57 | 0.2001002106 | 0.0667100310 | 0.0333554670 |
| 58 | 0.2002260260 | 0.0667170057 | 0.0333505470 |
| 59 | 0.2002510071 | 0.0667224452 | 0.0333642226 |
| 60 | 0.2002710607 | 0.0667270705 | 0.0333635307 |
| 61 | 0.2002000507 | 0.0667311020 | 0.0333655514 |
| 62 | 0.2003056645 | 0.0667345006 | 0.0333672040 |
| 63 | 0.2003102544 | 0.0667376146 | 0.0333600073 |
| 64 | 0.2003310461 | 0.0667402372 | 0.0333701106 |
| 65 | 0.2003444083 | 0.0667425072 | 0.0333712511 |
| 66 | 0.2003601006 | 0.0667444004 | 0.0333722316 |

FOR VALUE OF \$ = 00

| | 812 | 813 | 814 |
|----|---------------|--------------|--------------|
| 1 | 0.0100551977 | 0.0000630364 | 0.0000310102 |
| 2 | 0.0430552640 | 0.0001460107 | 0.0000734503 |
| 3 | 0.0710152462 | 0.0002370060 | 0.0001100534 |
| 4 | 0.0997302200 | 0.0003307542 | 0.0001653371 |
| 5 | 0.1250373277 | 0.0004210002 | 0.0002100501 |
| 6 | 0.1510005274 | 0.0005092110 | 0.0002546055 |
| 7 | 0.1765469015 | 0.0005914463 | 0.0002957231 |
| 8 | 0.1993070063 | 0.0006670407 | 0.0003330743 |
| 9 | 0.2204271257 | 0.0007394406 | 0.0003692243 |
| 10 | 0.2396761775 | 0.0008092025 | 0.0004044572 |
| 11 | 0.2571773529 | 0.0008761548 | 0.0004387874 |
| 12 | 0.2730107037 | 0.0009414664 | 0.0004723032 |
| 13 | 0.2872742712 | 0.0009952301 | 0.0005051060 |
| 14 | 0.3000700775 | 0.0010482001 | 0.0005372416 |
| 15 | 0.3115307057 | 0.0010992000 | 0.0005687400 |
| 16 | 0.3217673004 | 0.0011492064 | 0.0005997332 |
| 17 | 0.3308754061 | 0.0011984505 | 0.0006302200 |
| 18 | 0.3389602000 | 0.0012469741 | 0.0006602070 |
| 19 | 0.3461401035 | 0.0012947240 | 0.0006897430 |
| 20 | 0.3525040004 | 0.0013417201 | 0.0007189600 |
| 21 | 0.3581255674 | 0.0013880744 | 0.0007477747 |
| 22 | 0.3630092306 | 0.0014337352 | 0.0007762076 |
| 23 | 0.3674640404 | 0.0014787360 | 0.0008042504 |
| 24 | 0.37133100704 | 0.0015230510 | 0.0008319050 |
| 25 | 0.3747123400 | 0.0015667165 | 0.0008591600 |
| 26 | 0.3776045770 | 0.0016097872 | 0.0008860156 |
| 27 | 0.3803130320 | 0.0016523023 | 0.0009124712 |
| 28 | 0.3828127052 | 0.0016943023 | 0.0009385272 |
| 29 | 0.3851620561 | 0.0017358067 | 0.0009641834 |
| 30 | 0.3873050060 | 0.0017768547 | 0.0009894400 |
| 31 | 0.3892730707 | 0.0018174971 | 0.0010142960 |
| 32 | 0.3910850356 | 0.0018577827 | 0.0010387520 |
| 33 | 0.3927401300 | 0.0018977507 | 0.0010628080 |
| 34 | 0.3942483146 | 0.0019374500 | 0.0010864640 |
| 35 | 0.3956107053 | 0.0019768300 | 0.0011097200 |
| 36 | 0.3968284662 | 0.0020159440 | 0.0011325760 |
| 37 | 0.3979011120 | 0.0020548327 | 0.0011550320 |
| 38 | 0.3988387026 | 0.0020935501 | 0.0011770880 |
| 39 | 0.3996425347 | 0.0021321567 | 0.0011987440 |
| 40 | 0.4003127407 | 0.0021706000 | 0.0012199000 |
| 41 | 0.4008501350 | 0.0022088344 | 0.0012405560 |
| 42 | 0.4012606115 | 0.0022469070 | 0.0012607120 |
| 43 | 0.4015431044 | 0.0022847700 | 0.0012803680 |
| 44 | 0.4017072400 | 0.0023224730 | 0.0013005240 |
| 45 | 0.4017534502 | 0.0023599665 | 0.0013202800 |
| 46 | 0.4016820467 | 0.0023972905 | 0.0013406360 |
| 47 | 0.4014930267 | 0.0024344902 | 0.0013605920 |
| 48 | 0.4011870364 | 0.0024715146 | 0.0013801480 |
| 49 | 0.4007641360 | 0.0025083330 | 0.0014003040 |
| 50 | 0.4002340711 | 0.0025449954 | 0.0014200600 |
| 51 | 0.40000410744 | 0.0025814671 | 0.0014404160 |
| 52 | 0.4000770030 | 0.0026177952 | 0.0014603720 |
| 53 | 0.4000517605 | 0.0026539355 | 0.0014809280 |
| 54 | 0.4000166402 | 0.0026899277 | 0.0015010840 |
| 55 | 0.4000729746 | 0.0027257114 | 0.0015208400 |
| 56 | 0.4000210504 | 0.0027613352 | 0.0015401960 |
| 57 | 0.4000642000 | 0.0027968474 | 0.0015601520 |
| 58 | 0.4000100550 | 0.0028322407 | 0.0015807080 |
| 59 | 0.4000320033 | 0.0028675475 | 0.0016008640 |
| 60 | 0.4000650666 | 0.0029027403 | 0.0016206200 |
| 61 | 0.4000940003 | 0.0029378600 | 0.0016409760 |
| 62 | 0.4001055221 | 0.0029729405 | 0.0016609320 |
| 63 | 0.4001235525 | 0.0030079500 | 0.0016804880 |
| 64 | 0.4001391007 | 0.0030429334 | 0.0017006440 |
| 65 | 0.4001527500 | 0.0030778400 | 0.0017203000 |
| 66 | 0.4001646000 | 0.0031127000 | 0.0017404560 |
| 67 | 0.4001740000 | 0.0031475500 | 0.0017601120 |
| 68 | 0.4001810000 | 0.0031824000 | 0.0017802680 |

THE RESULT OF DISCRETE STATE AND CONTINUOUS TIME FOR WEIBULL
STARTS FROM THE NEXT PAGE

| 012 | 013 | 014 |
|---------------|--------------|---------------|
| 0.0424015714 | 0.0282677803 | 0.0141338002 |
| 0.0788103342 | 0.0525402203 | 0.0252701102 |
| 0.1100730374 | 0.0733020700 | 0.0365010100 |
| 0.1369170094 | 0.0912700607 | 0.0456300344 |
| 0.1599670640 | 0.1066447040 | 0.0533223525 |
| 0.1797501746 | 0.1198304440 | 0.0599107224 |
| 0.1967530744 | 0.1311602446 | 0.0655046223 |
| 0.2113465667 | 0.1400077052 | 0.0704480531 |
| 0.2238767504 | 0.1462511630 | 0.0746255015 |
| 0.2346350103 | 0.1554230413 | 0.0782110706 |
| 0.2438744150 | 0.1625020330 | 0.0812044670 |
| 0.2519071532 | 0.1678714305 | 0.08360357153 |
| 0.2586100076 | 0.1724124402 | 0.08562052201 |
| 0.2644574770 | 0.1763116410 | 0.0871550710 |
| 0.2694905064 | 0.1796507242 | 0.08800200521 |
| 0.2738010220 | 0.1825346053 | 0.08812673026 |
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| 14.3424195270 | 14.3424195270 | 14.3424195270 |
| 14.4347482770 | 14.4347482770 | 14.4347482770 |
| 14.5272870270 | 14.5272870270 | 14.5272870270 |
| 14.6200357770 | 14.6200357770 | 14.6200357770 |
| 14.7129945270 | 14.7129945270 | 14.7129945270 |
| 14.8061632770 | 14.8061632770 | 14.8061632770 |
| 14.8995420270 | 14.8995420270 | 14.8995420270 |
| 14.9931307770 | 14.9931307770 | 14.9931307770 |
| 15.0869295270 | 15.0869295270 | 15.0869295270 |
| 15.1809382770 | 15.180938277 | |

THE RESULT OF DISCRETE STATE AND CONTINUOUS TIME FOR
EXPONENTIAL STARTS FROM THE NEXT PAGE

| 0 | 012 | 013 | 014 |
|----|--------------|--------------|--------------|
| 1 | 0.0043220047 | 0.0562152565 | 0.0201076702 |
| 2 | 0.1140446002 | 0.0866707314 | 0.0403140657 |
| 3 | 0.1085270029 | 0.1256046637 | 0.0620423310 |
| 4 | 0.2100504362 | 0.1465729475 | 0.0732064730 |
| 5 | 0.2423050200 | 0.1615900240 | 0.0807050124 |
| 6 | 0.2503702542 | 0.1723061545 | 0.0861930773 |
| 7 | 0.2702216506 | 0.1801477622 | 0.0900730761 |
| 8 | 0.2703010320 | 0.185777602 | 0.0920030001 |
| 9 | 0.2040000100 | 0.1807303316 | 0.0940000000 |
| 10 | 0.2000350053 | 0.1720223010 | 0.0863110010 |
| 11 | 0.2020451462 | 0.164067001 | 0.0873403046 |
| 12 | 0.2042010055 | 0.1661073770 | 0.0880036005 |
| 13 | 0.2050005431 | 0.1672500230 | 0.088605110 |
| 14 | 0.2070441070 | 0.1680204435 | 0.0890147210 |
| 15 | 0.2070740071 | 0.1685033100 | 0.0897016500 |
| 16 | 0.2004722053 | 0.1690015006 | 0.0894007543 |
| 17 | 0.2000016771 | 0.1692677007 | 0.0896330040 |
| 18 | 0.2002103004 | 0.1694736046 | 0.0897360023 |
| 19 | 0.2004323273 | 0.1696215502 | 0.0898107701 |
| 20 | 0.2005010000 | 0.1697270376 | 0.0898630600 |
| 21 | 0.2007066001 | 0.1698044103 | 0.0899022052 |
| 22 | 0.200800711 | 0.1698503007 | 0.0899206004 |
| 23 | 0.2000403470 | 0.1698000006 | 0.0899404403 |
| 24 | 0.2000000050 | 0.1698273151 | 0.0899636576 |
| 25 | 0.2000216310 | 0.1698477505 | 0.0899730700 |
| 26 | 0.2000436557 | 0.1698624372 | 0.0899812106 |
| 27 | 0.2000505106 | 0.1698730021 | 0.0899865010 |
| 28 | 0.2000700051 | 0.1698805060 | 0.0899907034 |
| 29 | 0.2000700000 | 0.1698860106 | 0.0899920203 |
| 30 | 0.2000040617 | 0.1698800506 | 0.0899940700 |
| 31 | 0.2000010327 | 0.1698827000 | 0.0899963054 |
| 32 | 0.2000022325 | 0.1698840174 | 0.0899974007 |
| 33 | 0.2000044001 | 0.1698862777 | 0.0899981300 |
| 34 | 0.2000050006 | 0.1698873700 | 0.0899986604 |
| 35 | 0.2000071211 | 0.1698880550 | 0.0899990320 |
| 36 | 0.2000070250 | 0.1698880172 | 0.0899993006 |
| 37 | 0.2000005210 | 0.1698880046 | 0.0899995023 |
| 38 | 0.2000000300 | 0.1698882077 | 0.0899996430 |
| 39 | 0.2000002371 | 0.1698884063 | 0.0899997402 |
| 40 | 0.2000004457 | 0.1698886305 | 0.0899998152 |
| 41 | 0.2000006245 | 0.1698887340 | 0.0899998674 |
| 42 | 0.2000007130 | 0.1698888003 | 0.0899999046 |
| 43 | 0.2000008023 | 0.1698888540 | 0.0899999270 |
| 44 | 0.2000008920 | 0.1698888936 | 0.0899999460 |
| 45 | 0.2000009827 | 0.1698889285 | 0.0899999612 |
| 46 | 0.2000010723 | 0.1698889583 | 0.0899999701 |
| 47 | 0.2000011623 | 0.1698889732 | 0.0899999866 |
| 48 | 0.2000012521 | 0.1698889732 | 0.0899999866 |
| 49 | 0.2000013421 | 0.1698889732 | 0.0899999866 |
| 50 | 0.2000014321 | 0.1698889801 | 0.0899999940 |
| 51 | 0.2000015221 | 0.1698889801 | 0.0899999940 |
| 52 | 0.2000016121 | 0.1698889801 | 0.0899999940 |
| 53 | 0.2000000110 | 0.2000000030 | 0.1000000015 |
| 54 | 0.2000000110 | 0.2000000030 | 0.1000000015 |
| 55 | 0.2000000110 | 0.2000000030 | 0.1000000015 |
| 56 | 0.2000000110 | 0.2000000030 | 0.1000000015 |
| 57 | 0.2000000110 | 0.2000000030 | 0.1000000015 |
| 58 | 0.2000000110 | 0.2000000030 | 0.1000000015 |
| 59 | 0.2000000110 | 0.2000000030 | 0.1000000015 |
| 60 | 0.2000000110 | 0.2000000030 | 0.1000000015 |
| 61 | 0.2000000110 | 0.2000000030 | 0.1000000015 |
| 62 | 0.2000000110 | 0.2000000030 | 0.1000000015 |
| 63 | 0.2000000110 | 0.2000000030 | 0.1000000015 |
| 64 | 0.2000000110 | 0.2000000030 | 0.1000000015 |
| 65 | 0.2000000110 | 0.2000000030 | 0.1000000015 |
| 66 | 0.2000000110 | 0.2000000030 | 0.1000000015 |
| 67 | 0.2000000110 | 0.2000000030 | 0.1000000015 |

| S | 012 | 013 | 014 |
|----|--------------|---------------|--------------|
| 1 | 0.1264043345 | 0.0201076267 | 0.0140530141 |
| 2 | 0.2174160123 | 0.0403140657 | 0.0241574320 |
| 3 | 0.2027005110 | 0.0620423310 | 0.0314211650 |
| 4 | 0.3297001310 | 0.0732064730 | 0.0306432360 |
| 5 | 0.3635775447 | 0.0907050124 | 0.0403075062 |
| 6 | 0.3070000012 | 0.0901030773 | 0.0430065306 |
| 7 | 0.4053324750 | 0.0900730761 | 0.0450036300 |
| 8 | 0.4170074403 | 0.0900630001 | 0.0464316100 |
| 9 | 0.4260135206 | 0.0900606650 | 0.0474340320 |
| 10 | 0.4334025070 | 0.09003116010 | 0.0401550405 |
| 11 | 0.4300677342 | 0.0973463046 | 0.0406741023 |
| 12 | 0.4414216200 | 0.0900036005 | 0.0400460442 |
| 13 | 0.4430320147 | 0.0906705110 | 0.0403147550 |
| 14 | 0.4455666660 | 0.0900147310 | 0.0405073600 |
| 15 | 0.4460124007 | 0.0900016500 | 0.0406450200 |
| 16 | 0.4477004270 | 0.0904007543 | 0.0407453772 |
| 17 | 0.4493525157 | 0.0906300040 | 0.0409160474 |
| 18 | 0.4490156140 | 0.0907360023 | 0.0409604011 |
| 19 | 0.4491405357 | 0.0900107701 | 0.0400053005 |
| 20 | 0.4493070404 | 0.0900030000 | 0.0400310044 |
| 21 | 0.4495500270 | 0.0900022052 | 0.0400511026 |
| 22 | 0.449692364 | 0.0900006004 | 0.0400640452 |
| 23 | 0.4497725360 | 0.0900040103 | 0.0400747247 |
| 24 | 0.4498364035 | 0.0900036676 | 0.0400010700 |
| 25 | 0.4499024477 | 0.0900030700 | 0.0400060300 |
| 26 | 0.4499154005 | 0.0900031206 | 0.0400060003 |
| 27 | 0.4499002500 | 0.0900065010 | 0.0400032505 |
| 28 | 0.4498663277 | 0.0900003034 | 0.0400051467 |
| 29 | 0.4498000002 | 0.0900003003 | 0.0400065101 |
| 30 | 0.4497747777 | 0.0900040700 | 0.0400074000 |
| 31 | 0.4499037756 | 0.0900063054 | 0.0400001077 |
| 32 | 0.4499003354 | 0.0900074007 | 0.0400007043 |
| 33 | 0.4499016136 | 0.0900001300 | 0.0400006604 |
| 34 | 0.4499030600 | 0.0900006604 | 0.0400003302 |
| 35 | 0.4499056667 | 0.0900000320 | 0.0400005165 |
| 36 | 0.4499061004 | 0.0900003006 | 0.0400006543 |
| 37 | 0.4499077520 | 0.0900005023 | 0.0400007512 |
| 38 | 0.4499004006 | 0.0900006430 | 0.0400000210 |
| 39 | 0.4499008556 | 0.0900007402 | 0.0400000741 |
| 40 | 0.4499001034 | 0.0900000152 | 0.0400000076 |
| 41 | 0.4499004210 | 0.0900000074 | 0.0400000327 |
| 42 | 0.4499006006 | 0.0900000046 | 0.0400000023 |
| 43 | 0.4499005601 | 0.0900000270 | 0.0400000035 |
| 44 | 0.4499000003 | 0.0900000560 | 0.0400000704 |
| 45 | 0.4499000600 | 0.0900000642 | 0.0400000021 |
| 46 | 0.4499000007 | 0.0900000701 | 0.0400000006 |
| 47 | 0.4499000205 | 0.0900000066 | 0.0400000033 |
| 48 | 0.4499000503 | 0.0900000066 | 0.0400000033 |
| 49 | 0.4499000503 | 0.0900000066 | 0.0400000033 |
| 50 | 0.4499000001 | 0.0900000040 | 0.0400000070 |
| 51 | 0.4499000001 | 0.0900000040 | 0.0400000070 |
| 52 | 0.4499000001 | 0.0900000040 | 0.0400000070 |
| 53 | 0.4500000170 | 0.1000000015 | 0.0500000007 |
| 54 | 0.4500000170 | 0.1000000015 | 0.0500000007 |
| 55 | 0.4500000170 | 0.1000000015 | 0.0500000007 |
| 56 | 0.4500000170 | 0.1000000015 | 0.0500000007 |
| 57 | 0.4500000170 | 0.1000000015 | 0.0500000007 |
| 58 | 0.4500000170 | 0.1000000015 | 0.0500000007 |
| 59 | 0.4500000170 | 0.1000000015 | 0.0500000007 |
| 60 | 0.4500000170 | 0.1000000015 | 0.0500000007 |
| 61 | 0.4500000170 | 0.1000000015 | 0.0500000007 |
| 62 | 0.4500000170 | 0.1000000015 | 0.0500000007 |
| 63 | 0.4500000170 | 0.1000000015 | 0.0500000007 |
| 64 | 0.4500000170 | 0.1000000015 | 0.0500000007 |
| 65 | 0.4500000170 | 0.1000000015 | 0.0500000007 |
| 66 | 0.4500000170 | 0.1000000015 | 0.0500000007 |
| 67 | 0.4500000170 | 0.1000000015 | 0.0500000007 |

POB K= .00

| | 012 | 013 | 014 |
|----|---------------|--------------|---------------|
| 1 | 0.1670025424 | 0.0005621520 | 0.0002010760 |
| 2 | 0.2004207507 | 0.0006662064 | 0.0004031402 |
| 3 | 0.2751607407 | 0.0012560455 | 0.0006704220 |
| 4 | 0.4375207656 | 0.0014657202 | 0.0007320641 |
| 5 | 0.4072462050 | 0.0016150007 | 0.0008077472 |
| 6 | 0.5146726000 | 0.0017200500 | 0.0008610300 |
| 7 | 0.5377410650 | 0.0018014750 | 0.0009007270 |
| 8 | 0.5642073446 | 0.0018672757 | 0.0009206270 |
| 9 | 0.5663710177 | 0.0019073015 | 0.0009406050 |
| 10 | 0.5740007054 | 0.0019262310 | 0.0009601150 |
| 11 | 0.5011600437 | 0.0019460650 | 0.0009724020 |
| 12 | 0.5056103304 | 0.0019610720 | 0.0009802600 |
| 13 | 0.5000101025 | 0.0019725002 | 0.0009862041 |
| 14 | 0.5011170105 | 0.0019802026 | 0.0009901463 |
| 15 | 0.5027712321 | 0.0019850314 | 0.0009920157 |
| 16 | 0.5030500600 | 0.0019890133 | 0.0009940066 |
| 17 | 0.5040143601 | 0.0019926750 | 0.0009963300 |
| 18 | 0.5054207052 | 0.0019947312 | 0.0009979671 |
| 19 | 0.5050703756 | 0.0019962130 | 0.0009991060 |
| 20 | 0.5061070006 | 0.0019972774 | 0.0009996307 |
| 21 | 0.5064161754 | 0.0019980422 | 0.0009999211 |
| 22 | 0.5065002670 | 0.0019985010 | 0.0009999060 |
| 23 | 0.5066002245 | 0.0019989070 | 0.00099994035 |
| 24 | 0.5067030420 | 0.0019992713 | 0.00099996357 |
| 25 | 0.5068440771 | 0.0019994755 | 0.00099997370 |
| 26 | 0.5069070065 | 0.0019996224 | 0.00099998117 |
| 27 | 0.50690104174 | 0.0019997201 | 0.00099998641 |
| 28 | 0.5069420671 | 0.0019998030 | 0.00099999010 |
| 29 | 0.5069503302 | 0.0019998505 | 0.00099999203 |
| 30 | 0.5069700013 | 0.0019998976 | 0.00099999400 |
| 31 | 0.5069704056 | 0.0019999261 | 0.00099999630 |
| 32 | 0.5069845653 | 0.0019999463 | 0.00099999732 |
| 33 | 0.5069800164 | 0.0019999607 | 0.00099999804 |
| 34 | 0.5069820150 | 0.0019999712 | 0.00099999856 |
| 35 | 0.5069842000 | 0.0019999780 | 0.00099999895 |
| 36 | 0.5069850001 | 0.0019999843 | 0.00099999921 |
| 37 | 0.5069870226 | 0.0019999892 | 0.00099999941 |
| 38 | 0.5069870167 | 0.0019999910 | 0.00099999955 |
| 39 | 0.5069885127 | 0.0019999931 | 0.00099999966 |
| 40 | 0.5069880300 | 0.0019999945 | 0.00099999973 |
| 41 | 0.5069892200 | 0.0019999954 | 0.00099999977 |
| 42 | 0.50698974664 | 0.0019999961 | 0.00099999981 |
| 43 | 0.5069895056 | 0.0019999966 | 0.00099999983 |
| 44 | 0.5069897644 | 0.0019999971 | 0.00099999985 |
| 45 | 0.5069898240 | 0.0019999973 | 0.00099999987 |
| 46 | 0.5069898037 | 0.0019999975 | 0.00099999988 |
| 47 | 0.5069898433 | 0.0019999970 | 0.00099999990 |
| 48 | 0.5069898433 | 0.0019999980 | 0.00099999990 |
| 49 | 0.5069898433 | 0.0019999980 | 0.00099999990 |
| 50 | 0.5070000020 | 0.0019999980 | 0.00099999990 |
| 51 | 0.5070000020 | 0.0019999980 | 0.00099999990 |
| 52 | 0.5070000020 | 0.0019999980 | 0.00099999990 |
| 53 | 0.5070000020 | 0.0019999982 | 0.00099999991 |
| 54 | 0.5070000020 | 0.0019999982 | 0.00099999991 |
| 55 | 0.5070000020 | 0.0019999982 | 0.00099999991 |
| 56 | 0.5070000020 | 0.0019999982 | 0.00099999991 |
| 57 | 0.5070000020 | 0.0019999982 | 0.00099999991 |
| 58 | 0.5070000020 | 0.0019999982 | 0.00099999991 |
| 59 | 0.5070000020 | 0.0019999982 | 0.00099999991 |
| 60 | 0.5070000020 | 0.0019999982 | 0.00099999991 |
| 61 | 0.5070000020 | 0.0019999982 | 0.00099999991 |
| 62 | 0.5070000020 | 0.0019999982 | 0.00099999991 |
| 63 | 0.5070000020 | 0.0019999982 | 0.00099999991 |
| 64 | 0.5070000020 | 0.0019999982 | 0.00099999991 |
| 65 | 0.5070000020 | 0.0019999982 | 0.00099999991 |

APPENDIX D

The computational Procedures for the illustration of the Markov-Multi drugs decision processes for the Control of diseases.

We shall use these values to determine the best policies for every n , we have

$${}^1Q_1 = {}^1P_{11} {}^1R_{11} + {}^1P_{12} {}^1R_{12} + {}^1P_{13} {}^1R_{13}$$

$${}^1Q_1 = 0.6 \times 1 + 0.2 \times 1 + 0.2 \times 3 = 1.4$$

$${}^1Q_2 = {}^1P_{21} {}^1R_{21} + {}^1P_{22} {}^1R_{22} + {}^1P_{23} {}^1R_{23}$$

$${}^1Q_2 = 0.1 \times 2 + 0.6 \times 2 + 0.3 \times 3 = 2.3$$

$${}^1Q_3 = {}^1P_{31} {}^1R_{31} + {}^1P_{32} {}^1R_{32} + {}^1P_{33} {}^1R_{33}$$

$${}^1Q_3 = 0.1 \times 1 + 0.2 \times 2 + 0.7 \times 4 = 3.3$$

$${}^2Q_1 = {}^2P_{11} {}^2R_{11} + {}^2P_{12} {}^2R_{12} + {}^2P_{13} {}^2R_{13}$$

$${}^2Q_1 = 0.8 \times 1 + 0.1 \times 2 + 0.1 \times 2 = 1.2$$

$${}^2Q_2 = {}^2P_{21} {}^2R_{21} + {}^2P_{22} {}^2R_{22} + {}^2P_{23} {}^2R_{23}$$

$${}^2Q_2 = 0.6 \times 3 + 0.3 \times 2 + 0.1 \times 4 = 2.8$$

$${}^2Q_3 = {}^2P_{31} {}^2R_{31} + {}^2P_{32} {}^2R_{32} + {}^2P_{33} {}^2R_{33}$$

$${}^2Q_3 = 0.5 \times 3 + 0.4 \times 2 + 0.1 \times 1 = 2.4$$

Let ${}^0V_i = 0$ for $i = 1, 2, 3$. Then for $n = 1$ we find ${}^0V_i^{(1)} = \text{Min}_{1,2,3} {}^1Q_i$ and

hence

$$d_1^{(1)} = 2, d_2^{(1)} = 1 \text{ and } d_3^{(1)} = 2$$

Let ${}^0V_1^{(1)}$, ${}^0V_2^{(1)}$ and ${}^0V_3^{(1)}$ be the minimum earnings (cost) corresponding to $d_1^{(1)}$, $d_2^{(1)}$ and $d_3^{(1)}$. We have

$${}^0V_1^{(1)} = 1.2, {}^0V_2^{(1)} = 2.3 \text{ and } {}^0V_3^{(1)} = 2.4$$

For $n=2$, we have

$${}^0V_1^{(2)} = \text{Min}_{1,2,3} [{}^1Q_i + \sum_{j=1}^3 {}^1P_{ij} {}^0V_j^{(2-1)}]$$

$${}^k V_i^{(2)} = \text{Min}_{1,2} [{}^k Q_i + \sum_{j=1}^3 {}^k P_{ij} {}^0 V_j^{(1)}]$$

$$= \text{Min}_{1,2} [{}^k Q_i + {}^k P_{i1} {}^0 V_1^{(1)} + {}^k P_{i2} {}^0 V_2^{(1)} + {}^k P_{i3} {}^0 V_3^{(1)}]$$

$$\begin{aligned} i = 1, k = 1 \quad {}^1 V_1^{(2)} &= {}^1 Q_1 + {}^1 P_{11} {}^0 V_1^{(1)} + {}^1 P_{12} {}^0 V_2^{(1)} + {}^1 P_{13} {}^0 V_3^{(1)} \\ &= 1.4 + 0.6 \times 1.2 + 0.2 \times 2.3 + 0.2 \times 2.4 = 3.00 \end{aligned}$$

$$\begin{aligned} i = 1, k = 2 \quad {}^2 V_1^{(2)} &= {}^2 Q_1 + {}^2 P_{21} {}^0 V_1^{(1)} + {}^2 P_{22} {}^0 V_2^{(1)} + {}^2 P_{23} {}^0 V_3^{(1)} \\ &= 1.2 + 0.6 \times 1.2 + 0.3 \times 2.3 + 0.1 \times 2.4 = 2.85 \end{aligned}$$

$$\begin{aligned} i = 2, k = 1 \quad {}^1 Q_2 + {}^1 P_{21} {}^0 V_1^{(1)} + {}^1 P_{22} {}^0 V_2^{(1)} + {}^1 P_{23} {}^0 V_3^{(1)} \\ &= 2.3 + 0.1 \times 1.2 + 0.6 \times 2.3 + 0.3 \times 2.4 = 4.52 \end{aligned}$$

$$\begin{aligned} i = 2, k = 2 \quad {}^2 Q_2 + {}^2 P_{21} {}^0 V_1^{(1)} + {}^2 P_{22} {}^0 V_2^{(1)} + {}^2 P_{23} {}^0 V_3^{(1)} \\ &= 2.8 + 0.6 \times 1.2 + 0.3 \times 2.3 + 0.1 \times 2.4 = 4.45 \end{aligned}$$

$$\begin{aligned} i = 3, k = 1 \quad {}^1 Q_3 + {}^1 P_{31} {}^0 V_1^{(1)} + {}^1 P_{32} {}^0 V_2^{(1)} + {}^1 P_{33} {}^0 V_3^{(1)} \\ &= 3.3 + 0.1 \times 1.2 + 0.2 \times 2.3 + 0.7 \times 2.4 = 5.56 \end{aligned}$$

$$\begin{aligned} i = 3, k = 2 \quad {}^2 Q_3 + {}^2 P_{31} {}^0 V_1^{(1)} + {}^2 P_{32} {}^0 V_2^{(1)} + {}^2 P_{33} {}^0 V_3^{(1)} \\ &= 2.4 + 0.5 \times 1.2 + 0.4 \times 2.3 + 0.1 \times 2.4 = 4.16 \end{aligned}$$

We see that for $n = 2$

$$d_1^{(2)} = 2, d_2^{(2)} = 2 \text{ and } d_3^{(2)} = 2$$

with ${}^0 V_1^{(2)} = 2.85$, ${}^0 V_2^{(2)} = 4.45$ and ${}^0 V_3^{(2)} = 4.16$

For $n = 3$, we have

$${}^k V_i^{(3)} = \text{Min}_{1,2} [{}^k Q_i + {}^k P_{i1} {}^0 V_1^{(2)} + {}^k P_{i2} {}^0 V_2^{(2)} + {}^k P_{i3} {}^0 V_3^{(2)}]$$

$$\begin{aligned} i = 1, k = 1 \quad {}^1 V_1^{(3)} &= {}^1 Q_1 + {}^1 P_{11} {}^0 V_1^{(2)} + {}^1 P_{12} {}^0 V_2^{(2)} + {}^1 P_{13} {}^0 V_3^{(2)} \\ &= 1.4 + 0.6 \times 2.85 + 0.2 \times 4.45 + 0.2 \times 4.16 = 4.83 \end{aligned}$$

$$\begin{aligned} i = 1, k = 2 \quad {}^2 V_1^{(3)} &= {}^2 Q_1 + {}^2 P_{11} {}^0 V_1^{(2)} + {}^2 P_{12} {}^0 V_2^{(2)} + {}^2 P_{13} {}^0 V_3^{(2)} \\ &= 1.2 + 0.8 \times 2.85 + 0.1 \times 4.45 + 0.1 \times 4.16 = 4.34 \end{aligned}$$

$$i = 2, k = 1. \quad {}^1Q_2 + {}^1P_{21} {}^0V_1^{(2)} + {}^1P_{22} {}^0V_2^{(2)} + {}^1P_{23} {}^0V_3^{(2)}$$

$$= 2.3 + 0.1 \times 2.85 + 0.6 \times 4.45 + 0.3 \times 4.16 = 6.50$$

$$i = 2, k = 2. \quad {}^2Q_2 + {}^2P_{21} {}^0V_1^{(2)} + {}^2P_{22} {}^0V_2^{(2)} + {}^2P_{23} {}^0V_3^{(2)}$$

$$= 2.8 + 0.6 \times 2.85 + 0.3 \times 4.45 + 0.1 \times 4.16 = 6.26$$

$$i = 3, k = 1. \quad {}^1Q_3 + {}^1P_{31} {}^0V_1^{(2)} + {}^1P_{32} {}^0V_2^{(2)} + {}^1P_{33} {}^0V_3^{(2)}$$

$$= 3.3 + 0.1 \times 2.85 + 0.2 \times 4.45 + 0.7 \times 4.16 = 7.39$$

$$i = 3, k = 2. \quad {}^2Q_3 + {}^2P_{31} {}^0V_1^{(2)} + {}^2P_{32} {}^0V_2^{(2)} + {}^2P_{33} {}^0V_3^{(2)}$$

$$= 2.4 + 0.5 \times 2.85 + 0.4 \times 4.45 + 0.1 \times 4.16 = 6.02$$

$$d_1^{(3)} = 2, d_2^{(3)} = 2 \text{ and } d_3^{(3)} = 2$$

$$\text{with } {}^0V_1^{(3)} = 4.34, {}^0V_2^{(3)} = 6.26 \text{ and } {}^0V_3^{(3)} = 6.02$$

For $n = 4$

$${}^kV_i^{(n)} = \text{Min}_{1,2} [{}^kQ_i + {}^kP_{i1} {}^0V_1^{(3)} + {}^kP_{i2} {}^0V_2^{(3)} + {}^kP_{i3} {}^0V_3^{(3)}]$$

$$i = 1, k = 1. \quad {}^1Q_1 + {}^1P_{11} {}^0V_1^{(3)} + {}^1P_{12} {}^0V_2^{(3)} + {}^1P_{13} {}^0V_3^{(3)}$$

$$= 1.4 + 0.6 \times 4.34 + 0.2 \times 6.26 + 0.2 \times 6.02 = 6.46$$

$$i = 1, k = 2. \quad {}^2Q_1 + {}^2P_{11} {}^0V_1^{(3)} + {}^2P_{12} {}^0V_2^{(3)} + {}^2P_{13} {}^0V_3^{(3)}$$

$$= 1.2 + 0.8 \times 4.34 + 0.1 \times 6.26 + 0.1 \times 6.02 = 5.90$$

$$i = 2, k = 1. \quad {}^1Q_2 + {}^1P_{21} {}^0V_1^{(3)} + {}^1P_{22} {}^0V_2^{(3)} + {}^1P_{23} {}^0V_3^{(3)}$$

$$= 2.3 + 0.1 \times 4.34 + 0.6 \times 6.26 + 0.3 \times 6.02 = 8.30$$

$$i = 2, k = 2. \quad {}^2Q_2 + {}^2P_{21} {}^0V_1^{(3)} + {}^2P_{22} {}^0V_2^{(3)} + {}^2P_{23} {}^0V_3^{(3)}$$

$$= 2.8 + 0.6 \times 4.34 + 0.3 \times 6.26 + 0.1 \times 6.02 = 7.88$$

$$i = 3, k = 1. \quad {}^1Q_3 + {}^1P_{31} {}^0V_1^{(3)} + {}^1P_{32} {}^0V_2^{(3)} + {}^1P_{33} {}^0V_3^{(3)}$$

$$= 3.3 + 0.1 \times 4.34 + 0.2 \times 6.26 + 0.7 \times 6.02 = 9.20$$

$$i = 3, k = 2. \quad {}^2Q_3 + {}^2P_{31} {}^0V_1^{(3)} + {}^2P_{32} {}^0V_2^{(3)} + {}^2P_{33} {}^0V_3^{(3)}$$

$$= 2.4 + 0.5 \times 4.34 + 0.4 \times 6.26 + 0.1 \times 6.02 = 7.68$$

$$d_1^{(4)} = 2, d_2^{(4)} = 2 \text{ and } d_3^{(4)} = 2$$

$$\text{with } {}^0V_1^{(4)} = 5.9, {}^0V_2^{(4)} = 7.88 \text{ and } {}^0V_3^{(4)} = 7.68$$

For $n = 5$

$$\begin{aligned} i = 1, k = 1, & \quad {}^1Q_1 + {}^1P_{11} {}^0V_1^{(4)} + {}^1P_{12} {}^0V_2^{(4)} + {}^1P_{13} {}^0V_3^{(4)} \\ & = 1.4 + 0.6 \times 5.9 + 0.2 \times 7.88 + 0.2 \times 7.68 = 8.05 \end{aligned}$$

$$\begin{aligned} i = 1, k = 2, & \quad {}^2Q_1 + {}^2P_{11} {}^0V_1^{(4)} + {}^2P_{12} {}^0V_2^{(4)} + {}^2P_{13} {}^0V_3^{(4)} \\ & = 1.2 + 0.8 \times 5.9 + 0.1 \times 7.88 + 0.1 \times 7.68 = 7.48 \end{aligned}$$

$$\begin{aligned} i = 2, k = 1, & \quad {}^1Q_2 + {}^1P_{21} {}^0V_1^{(4)} + {}^1P_{22} {}^0V_2^{(4)} + {}^1P_{23} {}^0V_3^{(4)} \\ & = 2.3 + 0.1 \times 5.9 + 0.6 \times 7.88 + 0.3 \times 7.68 = 9.92 \end{aligned}$$

$$\begin{aligned} i = 2, k = 2, & \quad {}^2Q_2 + {}^2P_{21} {}^0V_1^{(4)} + {}^2P_{22} {}^0V_2^{(4)} + {}^2P_{23} {}^0V_3^{(4)} \\ & = 2.8 + 0.6 \times 5.9 + 0.3 \times 7.88 + 0.1 \times 7.68 = 9.47 \end{aligned}$$

$$\begin{aligned} i = 3, k = 1, & \quad {}^1Q_3 + {}^1P_{31} {}^0V_1^{(4)} + {}^1P_{32} {}^0V_2^{(4)} + {}^1P_{33} {}^0V_3^{(4)} \\ & = 3.3 + 0.1 \times 5.9 + 0.2 \times 7.88 + 0.7 \times 7.68 = 10.84 \end{aligned}$$

$$\begin{aligned} i = 3, k = 2, & \quad {}^2Q_3 + {}^2P_{31} {}^0V_1^{(4)} + {}^2P_{32} {}^0V_2^{(4)} + {}^2P_{33} {}^0V_3^{(4)} \\ & = 2.4 + 0.5 \times 5.9 + 0.4 \times 7.88 + 0.1 \times 7.68 = 9.27 \end{aligned}$$

$$d_1^{(5)} = 2, d_2^{(5)} = 2 \text{ and } d_3^{(5)} = 2$$

$$\text{with } {}^0V_1^{(5)} = 7.48, {}^0V_2^{(5)} = 9.47 \text{ and } {}^0V_3^{(5)} = 9.27$$

| | | | |
|-----|--------------|--------------|--------------|
| 80 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 81 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 82 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 83 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 84 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 85 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 86 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 87 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 88 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 89 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 90 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 91 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 92 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 93 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 94 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 95 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 96 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 97 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 98 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 99 | 0.5070000020 | 0.0010000002 | 0.0000000001 |
| 100 | 0.5070000020 | 0.0010000002 | 0.0000000001 |

